

JPRS-ULS-89-008

13 JUNE 1989



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JPRS Report—

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CONTENTS

13 June 1989

Biophysics

Artificial Eye Developed [TASS, 16 Mar 89] 1
Mechanism of Membranotropic Effect of Methylethyl(Silatrano-1-ylmethyl) Sulfonium Iodide
[I. G. Kuznetsov, M. M. Rasulov, et al.; DOKLADY AKADEMII NAUK SSSR, Vol 301 No 5, Aug 88] 1

Biotechnology

Somaclonal Variability Factors
[L. V. Cherezhanova, V. N. Ovchinnikova, et al.; DOKLADY AKADEMII NAUK SSSR,
Vol 301 No 5, Aug 88] 2

Genetics

Recombination in Drosophila in Space Flight
[L. P. Filatova, E. N. Vaulina, et al.; GENETIKA, Apr 88] 3

Immunology

Engineering Recombinant Variolovaccinia Virus Strain Containing Expressed Influenza
A Virus Hemagglutinin Gene
[R. A. Gibadulin, A. A. Lazarenko, et al.; VOPROSY VIRUSOLOGII, Vol 33 No 3, May-Jun 88] 4

Laser Bioeffects

Argon Laser Coagulation in Diabetic Macular Retinopathy
[A. D. Semenov, F. A. Romashenkov, et al.; OFTALMOLOGICHESKIY ZHURNAL, No 4, 1988] 5
Diabetic Macular Retinopathy: Advisability and Tactics of Preventive Laser Interventions.
Long-Term Observations
[Yu. A. Ivanishko, A. A. Bochkareva, et al.; OFTALMOLOGICHESKIY ZHURNAL, No 4, 1988] 5
Trans-Scleral Ruby Laser Photocoagulation in Retinal Detachment
[S. G. Legeza, I. N. Ganichenko; OFTALMOLOGICHESKIY ZHURNAL, No 4, 1988] 5

Medicine

Rare Heart Operation Performed in Lithuania [TASS, 25 Mar 89] 6
Treatment for Severe Burns
[Vladimir Sologub Interview; ADVANCES OF SCIENCE AND TECHNOLOGY, No 7, 10 Mar 89] 6
Atherosclerosis: Skin Test Diagnosis
[Yevgeny Razin; ADVANCES OF SCIENCE AND TECHNOLOGY, No 7, 10 Mar 89] 7

Nonionizing Radiation Effects

Otklik Collective Develops New Electromagnetic Medical Devices [TASS, 12 May 89] 9

Pharmacology, Toxicology

Reactivating and Cholinolytic Effect of Dipyroxime in the Myoneural Synapse of Warm-Blooded Animals
[R. A. Giniatullin, I. A. Shabunova, et al.; NEYROFIZIOLOGIYA, Vol 20 No 3, May-June 88] 10
Structural and Functional Changes in Different Sections of the Brain and Spinal Cord
Produced by Dioxacarb
[N. V. Kokshareva, L. N. Badayeva; FIZIOLOGICHESKIY ZHURNAL, Vol 34 No 3, May-Jun 88] 10

Physiology

Prospective Drug Against Alcoholism [Alexander Rykov; <i>ADVANCES OF SCIENCE AND TECHNOLOGY</i> , No 4, 10 Feb 89]	11
Dynamics of Vestibular Nystagmus During Neurogenic Stress [Yu. L. Bronshteyn, V. S. Raytsev; <i>FIZIOLOGICHESKIY ZHURNAL</i> , May-Jun 88]	12
Comparative Study of Nociceptive Reactions After Bradykinin Introduction Into Different Receptor Zones of Awake Animals [A. V. Panov; <i>PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA</i> , May-Jun 88]	12
Effect of Synthetic Leu-Enkephalin Analog, Dalargin, on Metabolism and Blood Supply of the Liver After Acute Blood Loss in Rats [G. K. Zoloyev, N. Ya. Kovalenko, et al.; <i>PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA</i> , May-Jun 88]	12

Public Health

Rural Population Morbidity As Determined By Patient Visit and Comprehensive Medical Examination Data [M. M. Rayevskiy, D. V. Tintyuk; <i>ZDRAVOOKHRANENIYE TURKMENISTANA</i> , No 11, Nov 88]	14
Problems in Developing Fee-Based Medical Care for the Public [V. V. Grishin, G. Yu. Shvyrkov; <i>SOVETSKAYA ZDRAVOKHRANENIYE</i> , No 11, Nov 88]	17
Results of a Census of Oncology Patients Who Were Treated in a Number of Permanent Medical Facilities in Leningrad in 1982 [V. M. Merabishvili, O. T. Dyatchenko, et al.; <i>VOPROSY ONKOLOGII</i> , Vol 34 No 10, Oct 88]	20
Concern Over Chernobyl Thallium Poisoning [V. Popkov; <i>SOTSIALISTICHESKAYA INDUSTRIYA</i> , 23 May 89]	26
Soviet Pharmaceutical Industry: Present State and Future Prospects [Valery Bykov Interview; <i>ADVANCES OF SCIENCE AND TECHNOLOGY</i> , No 3, 30 Jan 89]	29

Radiation Biology

G. A. Zedgenidze Reviews Book on Radioprotectors [G. A. Zedgenidze; <i>MEDITSINSKAYA RADIOLOGIYA</i> , Vol 33 No 11, Nov 88]	32
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Virology

Oligonucleotide Derivatives Complementary to Viral RNA Inhibit Reproduction of Tick-Borne Encephalitis Virus In Cell Culture [V. V. Pogodina, T. V. Frolova, et al.; <i>DOKLADY AKADEMII NAUK SSSR</i> , Vol 301 No 5, Aug 88]	33
Reproduction of Blue and Orange Iridoviruses of Aedes Aspicius Caspius In Bombyx Mori Larvae [Kh. K. Torybayev; <i>MIKROBIOLOGICHESKIY ZHURNAL</i> , Vol 50 No 3, May-Jun 88]	33
New Stage In AIDS Study [A. Ya. Kulberg; <i>PRIRODA</i> , No 5, May 88]	33
Antiviral Activity of Amyxin Incorporated Into Liposomes [S. S. Grigoryan, A. N. Simonov, et al.; <i>VOPROSY VIRUSOLOGII</i> , Vol 33 No 3, May-Jun 88]	34
Production and Properties of Monoclonal Antibodies to Pichinde Arenavirus [L. Ya. Kunitskaya, I. V. Malakhova, et al.; <i>VOPROSY VIRUSOLOGII</i> , Vol 33, No 3, May-Jun 88]	34

Artificial Eye Developed
18400428a Moscow TASS in Russian 16 Mar 89

[Text] Soviet astrophysicist Osherov and biologist Tadzhikov from Tadzhikistan, a Soviet Central Asian republic, have created a model eye with the same index of light refraction and other characteristics that are inherent in living matter.

The retina is substituted by a special film with a photo-receiver transmitting an image to a screen. Planned initially as a teaching aid, the device was meant to help forecast diseases. But inventors believe that the possibilities of their creation are even greater. The artificial eye, which also sees subjects in color, can be used in navigation and underwater.

UDC 577.3:547.245

**Mechanism of Membranotropic Effect of
Methylethyl(Silatran-1-ylmethyl) Sulfonium
Iodide**

18400053b Moscow DOKLADY AKADEMII NAUK
SSSR in Russian Vol 301 No 5, Aug 88 (manuscript
received 15 Feb 88) pp 1235-1237

[Article by I. G. Kuznetsov, M. M. Rasulov, M. S. Sorokin and S. K. Suslova, Irkutsk Institute of Organic Chemistry, Siberian Division, USSR Academy of Sciences; All-Union Scientific Research and Design Institute of the Meat Industry, Moscow]

[Abstract] Methylethyl(silatran-1-ylmethyl) sulfonium iodide (MSI) can regulate the intensity of peroxide free-radical oxidation of lipids, indicating its membrane-stabilizing effect. MSI is a structural biological membrane modifier, indirectly inhibiting membrane degradation processes, particularly in experimental stress situations. In studying the possible mechanism of the membranotropic effect of MSI on various membranes, the researchers examined the changes induced by MSI in, for example, the surface biopotential and the viscoelastic properties of bilayer lipid membranes. They hypothesize that the high dipole moment of the MSI molecule gives it strong acceptor properties, which is indicated by its high capacity for stereospecific sorption. As a result, the silatran molecule adsorbed in the lipid bilayer of the membrane can electrostatically interact with the polar groups of the proteins and lipids of the membrane, which, most probably, leads to stabilization of the membrane as well as the silatran molecule itself. When it is being adsorbed on the membrane, the MSI may shift the polar groups, which leads to a "thinning" of the membrane and to a reduction of its contractibility. The shifted "heads" of the lipids, plus additional electrostatic interaction between the MSI molecule and the membrane, hinder the penetration of peroxide radicals to the alkyl chains of the lipids. The researchers suggest that cytoplasmic cell membranes exposed to MSI are converted to a new quasiequilibrium state, with altered conformational transition properties and a new conformational state. Figures 4, references 14: 9 Russian, 5 Western.

UDC 575.143:6

Somaclonal Variability Factors

18400053a Moscow DOKLADY AKADEMII NAUK
SSSR in Russian Vol 301 No 5, Aug 88 (manuscript
received 21 Jan 88) pp 1224-1226

[Article by L. V. Cherezhanova, V. N. Ovchinnikova and
O. S. Melik-Sarkisov, All-Union Scientific Research
Institute of Agricultural Biotechnology, Moscow]

[Abstract] Elements, sources of carbon, vitamins and other compounds present in nutrient media during cultivation of plant cells sometimes have mutagenic effects, leading to production of altered forms, allowing tissue cultures to be used to produce genetically altered, so-called somaclonal forms, which can serve as initial materials for the selection process. Experiments were performed to determine the effect of various concentrations of saccharose on cell nuclei and the mitotic activity of potato root meristems in culture in vitro and in vivo

and of onions. Virus-free potato plants were grown in a culture medium with saccharose concentration of 2, 4, 6, 8, 10, and 12 percent until they developed roots 5 cm long, at which point they were placed in a Karna mixture. The onions were also kept in a saccharose solution until they began to root. Cell division was inhibited considerably in the potato plants grown in vitro from apical meristems. Chromosome aberration increased and the mitotic index decreased with increasing concentrations of saccharose. The 12 percent solution was lethal for the onions. A pronounced mutagenic effect was observed in the onion at all saccharose concentrations. The mutagenic effect in cells cultivated in vitro, the so-called somaclonal variability, may be caused by mutagenic factors present in the culture medium. In these experiments, saccharose had a mutagenic effect, although it is necessary for induction of potato minitubers. The mechanism of the mutagenic effect of saccharose is unknown. It is assumed that breaks in the chromosomes are responses to the increase in osmotic potential, similar to the effect of salt.

UDC 575.116.12:595.773.4

Recombination in Drosophila in Space Flight

18400055 Moscow GENETIKA in Russian
Vol 24 No 4, Apr 88 (manuscript received 26 Nov 86,
revised manuscript received 8 Jun 87) pp 760-762

[Article by L. P. Filatova, E. N. Vaulina, N. Sh. Lapteva
and T. Ya. Grozdova, Institute of General Genetics
imeni N. I. Vavilov, USSR Academy of Sciences, Moscow]

[Abstract] An experiment performed aboard the space-
craft "Cosmos-1667" revealed the effect of a 7-day space
flight on recombination frequency in chromosome 2 in
male *Drosophila melanogaster* fruit flies. The experiment

included a study of the effect of a change in the force of
gravity during centrifuging and klinostating [klinostat-
irovaniye] on the recombination process in *Drosophila*.
Data from the literature show that the frequency of
recombination in space flight increases somewhat in
some cases, remains unchanged in some cases, and
decreases in others. This experiment showed a decrease
in frequency of recombination, which was attributed to
factors such as the effect of microgravitation, vibrations,
heavy cosmic ions, the gas environment, and electromag-
netic oscillations. The model experiment on a centrifuge
showed that the effect of the increased force of gravity on
the frequency of recombination was not great enough to
explain the flight effects. References 10: 5 Russian, 5
Western.

UDC 578.821.51:578.54:571.832.1:578.52]:
[577.212.3:575.222.75]

Engineering Recombinant Variolovaccinia Virus Strain Containing Expressed Influenza A Virus Hemagglutinin Gene

18400058a *VOPROSY VIRUSOLOGII* in Russian
Vol 33 No 3, May-Jun 88 (manuscript received
3 Sep 87) pp 275-278

[Article by R. A. Gibadulin, A. A. Lazarenko, V. P. Yuferov, L. F. Lideman, G. F. Denisova, N. A. Grodnitskaya, L. V. Urvayev and V. M. Zhdanov (deceased), Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

[Abstract] Researchers engineered a recombinant variolovaccinia virus strain in which a hemagglutinin gene of an influenza A virus—strain Udorn/307/72 (H3N2)—

was incorporated. The study revealed a high degree of expression of the hemagglutinin gene in the infected cell culture and good immunogenic properties in animal bodies. The level of expression of influenza A hemagglutinin virus in cultures infected by the recombinant strain of the variolovaccinia virus was determined by enzyme immunoassay. The capacity of the recombinant strain to induce antibodies to influenza A virus hemagglutinin was confirmed by a single intracutaneous or intravenous injection of 1×10^8 BOE of the variolovaccinia virus into Chinchilla rabbits weighing 2.5-3 kg. The single injection produced in the rabbits, within 2 weeks, a high level of antibodies to the influenza hemagglutinin. Intravenous injection produced a greater immune response. The study showed the considerable promise of the use of recombinant strains of variolovaccinia virus to produce immune, monospecific, polyvalent antisera for practical purposes. Figure 1; references 7: 2 Russian, 5 Western.

UDC 617.735-002-02:616.633.66-085.849.19

Argon Laser Coagulation in Diabetic Macular Retinopathy

18400240a Odessa OFTALMOLOGICHESKIY
ZHURNAL in Russian No 4, 1988 (manuscript received
3 Nov 86) pp 207-209

[Article by A. D. Semenov and F. A. Romashenkov, senior scientific fellows, O. A. Plyukhova, junior scientific fellow, and O. P. Pankova, candidate of medical sciences, Moscow Scientific Research Institute of Eye Microsurgery]

[Abstract] A comparative analysis was conducted on the outcomes of diabetic retinopathy management either by laser photocoagulation in conjunction with conventional drug regimens, or with chemotherapy alone. The former category encompassed 131 patients (207 eyes) ranging in age from 18 to 52 years; the latter cohort consisted of 42 patients (63 eyes). Laser photocoagulation was performed either with argon laser M-900 or krypton laser M-920 with a power output of 100-350 mW, using 0.1-0.2 sec exposures and burn spots of 50-200 μ m. The followup period covered 2 to 5 years. Depending on the clinical condition and the mode of photocoagulation employed, coagulation in the area of the macula lutea, generally combined with peripheral or panretinal coagulation, led to abatement or complete elimination of exudative changes in 59.9 percent of the laser group. In the control group treated only with drugs, improvements were seen in 28.5 percent of the cases. These findings provide strong indication for more extensive use of laser photocoagulation in the treatment of diabetic retinopathies. Figures 2; references 8: 4 Russian, 4 Western.

UDC 617.736-002-02:616.633.66-085.849.19

Diabetic Macular Retinopathy: Advisability and Tactics of Preventive Laser Interventions.

Long-Term Observations

18400240b Odessa OFTALMOLOGICHESKIY
ZHURNAL in Russian No 4, 1988 (manuscript received
16 Dec 87) pp 210-213

[Article by Yu. A. Ivanishko, candidate of medical sciences, A. A. Bochkareva, professor, and N. E. Temirov, doctor of medical sciences, North Caucasian Ophthalmological Laser Center; Chair of Eye Diseases, No 1 Rostov Medical Institute]

[Abstract] Trials were conducted with argon laser photocoagulation as a preventive modality in the case of diabetic macular retinopathy. A group of 34 patients at

risk of diabetic retinopathy, without any indication of retinal edema or microcystic changes in the fovea and with a visual acuity in the range of 0.6 to 1.0, were subjected to preventive panretinal laser photocoagulation alone, or in combination with either horseshoe coagulation around the fovea, or with panmacular coagulation. Followup observations spanned 6-9.5 years. The respective incidences of macular edema in these three groups were approximately 37, 10, and 11 percent; incidences of microcystic changes were 12, 5, and 5 percent. A control group of 13 patients could be followed for only 3.2 years after conventional drug management in view of the onset of frank diabetic retinopathy, which called for the employment of laser photocoagulation. Laser treatment, in addition to its proven efficacy as a preventive modality, was observed to be free of any serious complications and did not lead to cataracts. References 20: 7 Russian, 13 Western.

UDC 617.735-007.281-084-085.849.19

Trans-Scleral Ruby Laser Photocoagulation in Retinal Detachment

18400240c Odessa OFTALMOLOGICHESKIY
ZHURNAL in Russian No 4, 1988 (manuscript received
6 Apr 87) pp 225-228

[Article by S. G. Legeza and I. N. Ganichenko, candidates of medical sciences, Odessa Order of the Red Banner of Labor Scientific Research Institute of Eye Diseases and Tissue Therapy imeni Academician V. P. Filatov]

[Abstract] Therapeutic trials were conducted with trans-scleral ruby laser photocoagulation for the prophylactic therapy of retinal detachment. The study was conducted with a Soviet OK-2 laser with the beam directed 10-12 mm from the limbus, depending on the localization of retinal pathology, using a chessboard pattern to cover the scleral projections of the degenerative foci. The treatment regimen consisted of 2 to 3 sessions, with delivery of a 0.4 to 0.45 J beam 10-15 times per session. The time interval between sessions was 1 to 3 days. Ten patients treated in this manner were monitored for 9 to 22 months. All showed full retention of vision, and none required further treatment. Thus, this approach was found as efficacious as transpupillary laser photocoagulation in the management of retinal degeneration localized between the ora serrata and the equator of the eye. Figures 2; references 26: 11 Russian, 15 Western

Rare Heart Operation Performed in Lithuania
18400428b Moscow TASS in Russian 25 Mar 89

[Text] (Vilnius)—Implantation of a defibrillator, an apparatus restoring rhythmic work of the heart, was performed at the Cardiosurgical Clinic in the city of Kaunas, Lithuania (a Baltic Soviet republic). Engineer Vladas Ceriauskas, 57, was the first Soviet patient on whom this operation was made. It was performed by Iurigs Bredikis, professor of the Kaunas Medical Institute and full member of the USSR Academy of Medical Sciences.

Electrodes, linked to a defibrillating device which was placed in a specially made inner pocket near the front abdominal wall, were implanted into the cardiac muscle of the patient. In the event of a sudden dangerous malfunction of the cardiac rhythm, the device automatically generates a powerful pulse stopping arrhythmia and restoring blood circulation.

The unique operation is a result of cooperation between Lithuanian cardiosurgeons and the Australian firm Tele-electronics, which produces these apparatuses. Bioengineer Petrus Hollander, the firm's representative, who was present at the operation, said that his firm got interested in the experience of Lithuanian cardiosurgeons in the sphere of electrocardiostimulation and original surgical methods worked out by Academician Bredikis, which help remove successfully foci of arrhythmia with cryogenic and laser technology.

Bredikis, who heads a major center of surgical treatment of complicated malfunction of cardiac rhythm, believes that the introduction of a defibrillator into the body is a new promising move in cardiosurgery. Therefore, a contract was signed with the Teleelectronics firm on joint development of electrodes with minimum losses of power and improvement of methods of their use.

Treatment for Severe Burns
18400446a Moscow ADVANCES OF SCIENCE AND TECHNOLOGY in English No 7, 10 Mar 89 pp 1-3

[Interview by Novosti Press Agency correspondent with Professor Vladimir Sologub, vice director of the A.V. Vishnevsky Institute of Surgery's Burn Center]

[Text] When an earthquake struck Armenia, the first flight to the disaster area carried, in addition to Health Minister Evgeny Chazov, staff members of the A.V. Vishnevsky All-Union Institute of Surgery's Burn Center. Upon arrival, they organized evacuation of fire victims who, fortunately, were few in number. Eleven most serious patients were flown to Moscow. It can now be said that their lives are out of danger. Yet a few years ago many of them would have been doomed: burns covering 40 per cent of the body were considered lethal at that time.

Professor Vladimir Sologub, center head, vice-director of the A.V. Vishnevsky Institute of Surgery's Burn Center, talks to a Novosti Press Agency correspondent about the methods of treatment developed at the All-Union Burns Center.

Question: To begin with, will you explain the danger of a deep and extensive burn?

Answer: First, it is a painful shock typical of any injury. But after the shock is disposed of, there appears a host of other things threatening the patient's life. We call the condition so developed a "burn disease".

Question: So what happens to the victim when the danger of a pain shock is eliminated?

Answer: There usually appears the specific burn shock typical of a thermal injury. Liquid from the blood circulating in the body filters out through the wound and accumulates in the tissues in the form of extensive edemas. The blood gets clotted, upsetting the circulation and supply of blood to vital organs, with oxygen starvation developing as a result. Not so long ago there were practically no means to combat such dangerous complications apart from blood transfusions. Now we have highly efficient blood substitutes, such as polyglukin, reopolyglukin, and oxyamal. These and other medicines, in addition to using custom-designed air-therapy installations, first developed and used at our center, are our main tool to deal with burn disease.

Question: At your treatment center air-therapy units seem to have entirely eliminated common dressing material: plan and gauze bandages, don't they?

Answer: As a matter of fact, we gave up all bandages, salves and aerosol films designed to protect extensive burnt areas against microbe attacks. Today medical equipment does duty for all of these. A burnt part of the body is now covered with an aerial "bandage" - a plastic packet, with heated and moist air circulating under it all the time. The rate of circulation and temperature are maintained by an electronic system.

...Professor Sologub took me on a conducted tour of the wards. My apprehensions to see dry and hardened bandages, and pain-torn faces, disappeared without a trace. There was peace and quiet in the rooms. Transparent bags of diverse forms, looking like air balloons, quivered above patients' beds. Patients are practically spared any sharp pains inevitable in applying and removing bandages. And this at the country's burn center which treats the most serious cases.

Question: It is difficult to imagine a more lenient treatment of a burn. But what is the mechanism of its curative effect?

Answer: To begin with, the air blowing over the wound acts as a sterile bandage: it is fed into the bag via a system of filters where it is thoroughly cleaned. Any transfer of microbes from one section of the skin to another is ruled out, because air layers in the stream do not mix. Each damaged part of the skin gets its "own" portion of the air. Second, under such conditions necrotic tissues stop suppurating and dry up more quickly. By means of our air-therapy installations we eliminate or nearly eliminate perhaps the greatest peril to the patient: self-poisoning of the body with decomposition products of the wound's dead tissues.

Question: Why did you stress the word "nearly"?

Answer: The point is that necrotic tissues take rather long to dry up: as a rule, the process is completed on the fifth or sixth day of treatment. It is only then that they are removed surgically, and suturing is done. This is followed by a plastic operation of skin defects.

Question: Does your center transplant donor's skin?

Answer: It is more efficient to use the patient's own skin, if, of course, there is a place on his body from which it can be taken. As for donor's skin, we have abandoned this practice: we use instead a substitute - specially treated animal skin called "xenoskin". It fulfills protective functions as well as the donor's skin.

...Vladimir Sologub and myself continued our round of the wards. And I became increasingly convinced that treatment with sterile air does indeed produce amazing results. The original air-therapy units are used with maximum efficiency. There is a whole family of them here, several different modifications. In each case, the apparatus is adapted to specific purposes. For example, a stationary unit ATU-3 is designed to treat simultaneously five people with slight burns. The portable ATU-5 model is intended for one patient only. There is a specially designed unit to treat legs and feet. There also is an installation for whole-body treatment.

Question: Are your units used abroad?

Answer: Our installations have been bought in Hungary and Bulgaria. They are patented in Japan, West Germany, Italy and other countries.

Question: Judging by everything, air-therapy units have brought about a revolution in burn treatment, haven't they?

Answer: Yes, they have but it would be wrong to ascribe the success only to these designs. Of equally importance in treating extensive burns is an apparatus for lengthy tube feeding. The matter is that patients with deep burns lose a lot of tissue, plasma and other proteins. In addition to making up for the losses, we also must provide the body with all it needs for wound healing. Protracted intravenous feeding is fraught with complications. We

have solved the problem with the help of this apparatus: we feed our patients through a very fine gastric tube with specially developed and Soviet-made canned mixture Kombustal. Incorporation of this method into the treatment procedure makes it possible to cure people who have more than 50 per cent of their skin surface affected by deep burns and who lost over 30 per cent in weight. It was virtually impossible to save such people formerly. However, survival of patients depending on the percentage of burnt body surface is no more than a strategic guideline.

The professor took me to the bed of a young woman.

"This patient was brought to us from Ashkhabad. Burns covered 80 per cent of her body. Following a long period of treatment in air-therapy installations and six transplant operations we have been able to restore her skin. Now she is practically healthy and is soon to be discharged."

"And this patient," said the professor, slightly opening the door to the next ward, "had a relatively small area of burns, but saving her cost us tremendous efforts. In a fire she got her legs and abdomen burnt and, besides, she had to jump out of a window on the fourth floor. On top of the burns, she had both legs broken. One leg had to be amputated because of the onset of gangrene. The abdomen's burns were so bad that the stomach wall was impaired, with gastric juice entering the wound and corroding it. To arrest the process that threatened her life, we had to stop the secretion of gastric juice for a few days by means of medicines. That was enough to cope with the formidable danger."

To sum up. In every specific case, success of treatment depends on the doctor's art and skill in using tactical means available to him in the arsenal of medicine.

Interview recorded by Alexander Velikorechin.

Atherosclerosis: Skin Test Diagnosis

18400446b Moscow ADVANCES OF SCIENCE AND TECHNOLOGY in English No 7, 10 Mar 89 pp 1-2

[Article by Yevgeny Razin]

[Text] More than half the people on earth of the age between 35 and 55 die from infarctions, insults and gangrene of extremities caused by atherosclerosis (a hardening and degeneration of arterial walls). Since, unfortunately, no effective cure has as yet been found for the disease, its prevention and early diagnosis are particularly important. To be able to define what kind of assistance every person needs, the entire population has to be tested. But this cannot be done promptly with the means at our disposal now. The proximate methods of diagnosing atherosclerosis developed at the Institute of

Physicochemical Medicine of the Academy of Medical Sciences in Moscow make it possible to carry out effective tests which take no more than a few minutes to carry out.

"Screening tests to establish the heightened content of fats causing atherosclerosis—cholesterol and triglycerides—make it possible to quickly examine large groups of the population and to detect among them sick people and high-risk groups," says Academician Yuri Lopukhin, director of the Institute of Physicochemical Medicine. "Depending on the results obtained, we prescribe the necessary preventive measures and treatment."

"It is important to detect the disease at its initial stage. Some people can be helped by specially prescribed diets restricting these fats, others by exercises, massage and acupuncture. We know a sufficient number of means to prevent the disease from further developing. And this is most important, for when the vessels are no longer able to perform their functions, a complete cure is practically ruled out."

"When working out the proximate diagnosis methods we considered it most important that they be simple and within the reach of every in- and out-patient clinic. Even mobile clinics could in future be used for this purpose."

Skin Test to Indicate Cholesterol Content

The test is done in the following way: three drops of a special solution of different concentration (its composition is the invention), which responds to the presence of cholesterol in the skin cell membranes are put on the patient's palm. A minute later they are removed by a wad and a developer is applied to the same spots. A minute later the drops acquire a color, the intensity of which shows the cholesterol content. If only one drop becomes colored and the other two remain as they were, it means that the patient is healthy; if two are colored, he is in the risk group, and if three, he is sick and consequently needs a more thorough examination and urgent aid.

"The method is based on the well-known fact of the proportional correlation of cholesterol accumulated by the skin cell membranes and its overall amount in the body. What we did find is a substance that "takes well" to the skin and binds with the cholesterol. If we used traditional means to find this correlation we would have to make a chemical test of a piece of a patient's skin. But this procedure takes several days and is rather painful, too."

The skin tests carried out in clinics on different groups of patients, including people with diagnosed atherosclerosis showed its high efficiency.

Fluorescence to Diagnose the Disease

This method, which is based on an analysis of blood plasma, makes it easy to detect lipid metabolism disorders determining the early stages of the development of atherosclerosis. A drop of blood serum is put in a test-tube with a buffer solution, and then another drop with a fluorescent dye is added to it. After that the test-tube is placed into the electromagnetic chamber of a device that is connected with a computer display. A click of the tumbler and figures immediately begin to appear on the display showing the overall cholesterol and triglyceride content in the blood serum.

"All we need for a screening test according to our method," says Yevgeny Lapshin from the laboratory of biophysical diagnosis methods, "is five microlitres of blood taken from the patient's finger, or serum or plasma. Its mechanism is very simple: the intensity of the fluorescence dye's glow in the electromagnetic field depends upon the lipoid content in the solution. And this is what the computer translates into the language of figures."

"It is important to note," continued Yevgeny Lapshin, "that the test immediately indicates the content of two components responsible for the early development of atherosclerosis—cholesterol and triglycerides. And that makes it possible for the analysis to become finer and consequently more exact. The existing methods of diagnosis are capable of detecting only one of the components, mainly cholesterol. But studies of the development of atherosclerosis done, for example, in Scandinavian countries, have shown that an excess of triglycerides speeds up the development of the disease, too."

"Apart from that, three of four enzymes (each with specific properties) are generally used to identify the component. Then a photocalorimeter is used for determining the composition of the preparation from its color. However, this test is rather expensive to carry out. Our method is much cheaper."

The proximate method of diagnosing atherosclerosis by means of a fluorescent dye has successfully passed clinical tests in the USSR and is beginning to be applied in medical practice.

(APN)

Otklik Collective Develops New Electromagnetic Medical Devices

*18400445 Moscow TASS in Russian
1320 GMT 12 May 89*

[Text] An international conference under the title "Fundamental and Applied Aspects of the Use of Millimeter-Band Electromagnetic Radiation in Medicine" ended in Kiev today. The delegates heard and discussed several hundred scientific papers, analyzing, among other things, previously unknown communication channels between the human body and an electromagnetic field.

The Kiev-based creative collective Otklik has treated and cured more than 1,000 patients with the help of millimeter-band radiation. When a stream of waves is

directed against acupuncture points, a response is aroused in the vicinity of a diseased organ. Repeated a certain number of times, the procedure can cure the disease.

The Yerevan branch of Otklik has devised a device named "Diana," which makes it possible to identify acupuncture points in the human body: they begin to emit light when bombarded with radio waves. This device is a world first. Another device named "Sova" diagnoses the patient's condition by the strength of the points' luminescence.

Otklik's head, Prof Sergey Sitko, says that radiation can be used to cure such disorders as alcoholism and drug addiction, as well as for anti-cancer prophylaxis.

UDC 612.815:616—003.725

Reactivating and Cholinolytic Effect of Dipyroxime in the Myoneural Synapse of White-Blooded Animals

18400056 Kiev NEYROFIJOLOGIYA in Russian
Vol 20 No 3, May-Jun 88 (manuscript received
28 Apr 87) pp 351-357

[Article by R. A. Giniatullin, I. A. Shabunova, Ye. N. Nikolskiy and E. A. Bukharayeva, Kazan Medical Institute imeni S.V. Kurashov, RSFSR Ministry of Public Health]

[Abstract] Dipyroxime is an effective agent for treatment of poisoning with organophosphorus compounds which inhibit acetylcholinesterase (ACE). This article presents an evaluation of the ability of dipyroxime to reactivate phosphorylated ACE in the rat myoneural synapse and a study of the mechanism of the cholinolytic activity of dipyroxime. Experiments performed on isolated rat muscle preparations indicated that dipyroxime has both reactivating and cholinolytic effects in muscle with inhibited ACE, the ranges of effective concentrations being practically the same in both cases. The cholinolytic effect can substantially supplement the reactivating influence when ACE is inhibited. Complete reactivation is achieved at 2.5×10^{-4} mol/l dipyroxime. The cholinolytic effect apparently is stronger with inhibited ACE than with intact ACE, since the blocking of open ionic channels is stronger, the more the receptor-channel complexes are activated. Figures 6, references 14: 3 Russian, 11 Western.

UDC 615.9-0.85.7

Structural and Functional Changes in Different Sections of the Brain and Spinal Cord Produced by Dioxacarb

18400065a FIZIOLOGICHESKIY ZHURNAL in Russian Vol 34 No 3, May-Jun 88 (manuscript received 30 Mar 87) pp 27-32

[Article by N. V. Kokshareva and L. N. Badayeva, All-Union Institute of Hygiene and Toxicology of Pesticides, Polymers and Plastics, USSR Ministry of Health, Kiev]

[Abstract] The lack of data on the central effects of carbamates prompted researchers to study the ability of carbamate pesticides to penetrate to the central nervous system and affect the functional state of the brain and change the ultrastructure of the spinal cord. In a model for poisoning animals with dioxacarb, experiments were performed on 60 white rats of both sexes (weight 180-230 g) and 12 rabbits (weight 2.0-2.5 kg). The mean lethal dose (LD_{50}) of dioxacarb in peroral administration was determined with the least squares method for probit-analysis of lethality curves calculated by the Prozorovskiy method. The central action of carbamate was assessed from the change in functional state and ultrastructure of the spinal cord of the rats and from acetylcholinesterase activity in different sections of rabbit brain. The orally administered dioxacarb was highly toxic, with LD_{50} at 50 mg/kg for the rats and 10 mg/kg for the rabbits. In acute poisoning, the animals died within 30-40 minutes. The ability of carbamate pesticides to penetrate the blood-brain barrier and inhibit acetylcholinesterase activity in the studied sections of the brain was found to play a fundamental role in the mechanism of their toxic action. The level of suppression of acetylcholinesterase was at 65-78 percent, compared with controls, within 30 minutes in the rabbits and at 68 percent within the same period of time in the rats. One of the components of pathology is the increase of excitability of motor neurons in the initial period of action, with subsequent disturbance of the ultrastructure of nerve fibers and spinal column neurocytes, which indicates the direct toxic effect of carbamates on the central nervous system conduction apparatus. Figures 3; references 17: 13 Russian, 4 Western.

Prospective Drug Against Alcoholism
18400448 Moscow ADVANCES OF SCIENCE AND
TECHNOLOGY in English No 4, 10 Feb 89 pp 1-3

[Article by Alexander Rykov, Candidate of Medical Sciences]

[Text] A theory explaining mechanisms of the emergence of alcoholism has been evolved at the Anokhin Institute of Normal Physiology (USSR Academy of Medical Sciences). New approaches to studying the appearing predilection for alcohol opened up an opportunity to search in a purposeful way for drugs against this dangerous condition.

Academician Konstantin Sudakov, director of the Institute of Normal Physiology, had put forward an idea which in many years led to quite unexpected results. The idea is that a predilection for alcohol is determined by motivation. Being pathological in nature, it proceeds in accordance with neurobiological regularities typical of already studied motivations of other types (for instance, hunger, thirst, etc.).

If this is correct, nerve cells responsible for the emergence of alcoholic motivation must exist, and they can be discovered in the hypothalamus. This subcortical formation of the brain is small in size, but it plays a specific role in the functioning of the central nervous system. The hypothalamus is a link between our internal organs and consciousness. For instance, the cells of the hypothalamus are the first in the brain to react to the reduction of the level of nutrients in blood. As soon as this level falls below the critical mark, the cells send signals: "It is high time to search for food." Other cells of the hypothalamus are sensitive to the liquid content in the body and signalize thirst. Still other cells react to the changes in the content of sex hormones.

Motivations are impossible without the hypothalamus. If, for instance, the hunger centers are destroyed in it, an animal will die of exhaustion before a full feeding trough. On the contrary, the stimulation of these centers compels animals to eagerly take food even if they have just eaten.

What happens to alcoholics' hypothalamus? Researchers have assumed that constant abuse of alcohol alters metabolism of some cells of the hypothalamus so that alcohol becomes an indispensable component for them—its lack excites these cells, compels them to demand that the brain should find the way to satisfy alcoholic motivation, i.e., to seek alcohol.

No matter how small is the hypothalamus as compared with the remaining brain, it includes millions of neurons. How can neurons responsible for alcoholic motivation be found here? Researchers argued this way. Alcoholic predilection is satisfied by consumption of beer, vodka, and wine—in general, liquid. Hence, neurons—initiators of thirst—could acquire the properties of initiators. It is

convenient for the "alcoholic center" to settle in these neurons because they already have the experience in exciting the brain for searching and consuming liquids.

Some observations in our everyday life indirectly buttress the community of properties of cells responsible for the emergence of alcoholic and drinking motivations. After considerable intoxication many people experience strong thirst. Cucumber pickle is especially liked by drunkards. This is no accident since it contains liquid needed by the human body and salt which retains liquid in organs.

The center of thirst lies in supraoptical and paraventricular nuclei of the hypothalamus. When they are destroyed animals drink to a much lesser extent, and electric stimulation of these nuclei intensifies thirst. Perhaps cells provoking alcoholic motivation are situated here.

Scientists used a rather cruel method of turning normal rats into alcohol addicts. For a month rats were given only a 20-per cent spirit solution to drink. Then they were offered a chance to choose water or alcohol. Only seven out of 90 rats preferred water. Others turned into real alcoholics.

When the thirst center was stimulated by electric pulses in these alcoholic rats through fine wires implanted into the hypothalamus, the rats immediately began searching and eagerly drinking the alcoholic solution. The stimulation of thirst centers compelled the rats which preferred water to search for the feeding-trough, but with water—not with alcohol. When thirst centers of alcoholic rats were destroyed (rather the center of predilection for alcohol formed in its place) their thirst for alcohol began vanishing. Rats with the predilection for water drank less water after a similar operation. This has buttressed the hypothesis that a part of structures of the thirst center in animal alcoholics turn into the stimulant of alcoholism.

At first sight it seems that a direct road has opened towards a radical treatment of alcoholics: suffice it to destroy some sections of the thirst center, and alcoholic motivation will disappear. But everything is not so simple. The destruction of brain structures is a complex operation. It can be argued that alcoholism is a deadly dangerous conditions, and that, therefore, such operation could be justified. World practice has experience in destroying small brain structures for saving patients from fits of epilepsy, pathological aggressiveness and unbearable pain.

But surgical treatment is always an extreme measure. Is there an alternative? It has turned out that some chemical substances can influence the thirst center's cells regenerated into alcoholism initiator. A team of the institute's research associates, headed by Dr Alexander Kotov, has established that some peptides (biologically active compounds representing short chains of amino acids) can well make up the drug.

It has been known for long that some peptides regulate the hypothalamus' functioning. For instance, the peptide angiotensin-II selectively excites the thirst center and increases water consumption. Scientists have introduced it into the brain of rat alcoholics. This stimulated hunger, sexual and many other reactions, but not the search for water. Why? Apparently neurons of the thirst center in rat alcoholics acquire other properties than normal thirst cells. At the same time, after a single introduction of several micrograms of angiotensin-II the rats began drinking much less alcohol. The effect of angiotensin on the rats was relatively long—up to two weeks.

This is a very encouraging observation. It has enabled clinical tests of the new approach to medical treatment, but its wide introduction into practice will take a lot of time. Even if angiotensin becomes a new drug against alcoholism, it certainly will not save the world from boozers. Alcoholism is a social ailment and medical measures are of an auxiliary role in combating it. But this drug can play a prominent role. That's why today we need the search for effective means of helping people abusing alcohol and the study of the neurobiological mechanisms of shaping the dangerous dependence on it.

Studies by Moscow scientists have revealed the opportunity to choose substances selectively influencing the alcoholic predilection center. The result of the studies are important, of course, but it is also important that in the complex brain a cluster of neurons has been clearly detected and localized. Thus, neurons can serve as targets for such substances.

(APN)

UDC 612.886:616.45

Dynamics of Vestibular Nystagmus During Neurogenic Stress

18400065b *FIZIOLOGICHESKIY ZHURNAL* in Russian Vol 34 No 3, May-Jun 88 (manuscript received 27 Feb 87) pp 59-63

[Article by Yu. L. Bronshteyn and V. S. Raytsev, Ivanovo-Frankovsk Medical Institute, UkrSSR Ministry of Health]

[Abstract] A study of the dynamics of vestibular response in a realistic model of neurogenic stress involved chronic experiments on 18 rabbits subjected to neurogenic stress by the use of a "conflict of afferent excitations" type of model. The rabbits were stimulated with light, sound, and electric shock. Electronystagmography indicated that acute neurogenic stress alleviated rotatory and post-rotatory nystagmus. Chronic stress (daily for two hours, for five and ten days) also alleviated nystagmus, but to a lesser degree. Their autonomic (cardiac and respiratory) components were similarly affected. Changes of vestibular reactions were attributed to disturbances of systemic central and peripheral mechanisms of regulation of the vestibular system. Figures 2; references 15: 12 Russian, 3 Western.

UDC 615.357:577.175.853.015.4.076.9

Comparative Study of Nociceptive Reactions After Bradykinin Introduction Into Different Receptor Zones of Awake Animals

18400066a *Moscow PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA* in Russian No 3, May-Jun 88 (manuscript received 23 Apr 87) pp 9-11

[Article by A. V. Panov, 1st Leningrad Medical Institute imeni I. P. Pavlov, Department of Pharmacology]

[Abstract] A comparative analysis of emotional-behavioral and hemodynamic response in awake rats administered gradually increasing doses of bradykinin in the receptor zone of the heart and back leg vessels involved 40 narcotized rats with a catheter implanted into the right atrium and another at the bifurcation of the abdominal section of the aorta. Bradykinin was introduced by bolus in doses of 1, 2, 5, 10 and 50 µg in a volume of less than 1 µl. Emotional and motor manifestations evoked by the bradykinin were assessed visually, and arterial pressure in the carotid artery was recorded. The studies permitted development of a scale of emotional-behavioral response developing after introduction of bradykinin. The response to the introduction of bradykinin into different receptor zones was basically uniform. The bradykinin produced nociceptive emotional-behavioral responses similar to responses accompanying other forms of pain. This suggested that introduction of bradykinin into the heart may be a comparatively simple method of modelling cardiogenic pain in awake animals. The method has high stability of reproduction of both threshold and generalized nociceptive responses after repeated administrations of bradykinin. Figure 1; references 10: 5 Russian, 5 Western.

UDC 616-005.1-036.11-06:616.36-005.1-085.31: [547.95.547.943]-092.9-036.8-07:616.36

Effect of Synthetic Leu-Enkephalin Analog, Dalargin, on Metabolism and Blood Supply of the Liver After Acute Blood Loss in Rats

18400066b *Moscow PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA* in Russian No 3, May-Jun 88 (manuscript received 3 Apr 87) pp 48-52

[Article by G. K. Zoloyev; N. Ya. Kovalenko and D. D. Masiyevskiy, All-Union Scientific Center, Siberian Branch, USSR Academy of Medical Sciences, Pathophysiology Laboratory, Tomsk; Scientific Research Institute of General Pathology and Pathological Physiology, USSR Academy of Medical Sciences, Laboratory of Physiology of Extreme States]

[Abstract] A study of the effect of a new domestic dalargin preparation on liver metabolism and blood supply involved an experiment on 126 white male rats

(weight 180-250 g). Anesthetized rats (69), catheterized in the right common carotid artery, underwent acute blood loss of 3 percent of their body weight, after awakening. The rats were decapitated 1 or 3 hours after the blood letting. The control group included 15 rats. Urea and glucose concentration was determined in blood plasma. Glycogen level and ATP, ADP and AMP concentrations were determined in liver tissue samples. Microcirculation in the liver and intestines was studied in 42 rats under general urethane anesthesia. Visual study of the liver-intestine microcirculation was accompanied by measurement of the volumetric rate of blood flow in the portal vein and the linear rate of blood flow in the hepatic artery. Dalargin (500 μ g/kg), dissolved in 0.2 ml of normal saline, was injected into the femoral vein of the second group within 10 minutes after the cessation of blood loss. Blood loss increased glucose and

lactate levels in group 1 rats within 1 hour after acute blood loss and decreased the glycogen level in the liver, while the urea level in blood plasma was practically unchanged. Glucose and urea levels in the second group were essentially the same after 1 hour, but lactate was somewhat lower. All the animals with uncompensated blood loss died within the first hour of the experiment. Dalargin administration produced an increase of glycogen concentration in the liver, reduced glucose and lactate levels in the blood, and increased blood pressure and rate of hepatic blood flow in the animals with uncompensated hemodynamic disturbance. It increased the length of the compensation phase in those with compensated type. Mechanisms of the beneficial effect of Dalargin on hepatic metabolism and blood supply after acute blood loss were described and discussed. Figure 1; references 18: 14 Russian; 4 Western.

UDC 614.2(-22)+616-0.36.2

Rural Population Morbidity As Determined By Patient Visit and Comprehensive Medical Examination Data
18400270 Ashkhabad ZDRAVOKHRANENIYE TURKMENISTANA in Russian
No 11, Nov 88 pp 33-37

[Article by M. M. Rayevskiy and D. V. Tintyuk, Department of Social Hygiene and Health Care Administration, Kishinev State Medical Institute]

[Text] The new forms of health care planning and management must provide for an intensification of all activities at medical institutions. The intensification is defined primarily by a broad deployment of preventive measures, a step-wise introduction of universal mass health screening, and the realization of the "Comprehensive Program for Better Disease Prevention and Improved Health of the Rural Population."³

These problems can be resolved successfully within the framework of the entire health sector only if we have contemporary, scientifically substantiated, reliable information about the level and structure of public morbidity rates as determined by data on patient visits and comprehensive medical examinations, particularly in the rural areas,¹⁻⁴ since the quantitative and qualitative aspects of those factors have been studied the least in the rural regions.

The purpose of the present work is to establish the true level of the overall morbidity rate as determined by data involving patient visits and comprehensive medical examinations of rural residents under conventional and

experimental conditions; to determine the age-sex characteristics of morbidity distribution among rural residents; to identify an objective basis for determining the differentiated need for medical (including rehabilitation and mass health screening) and sanitarium-health resort assistance, as well as for the purpose of preventing illnesses.

In that connection we studied morbidity rates on the basis of data on patient visit and comprehensive medical examination reports in seven villages from five rural rayons of the republic that are typical for the four economic-geographic zones of the Moldavian SSR. Our selection of the population points and rayons took into consideration specialization of agriculture, the level of toxic chemical use, the number of residents and its age-sex composition, demographic factors, the availability of medical services and medical personnel, etc. Turnover data were based on a total of 26,950 individuals, whereas comprehensive medical examination data were based on 11,750 individuals.

The results of the study showed that the average morbidity level as determined by rural population patient visits over a three year period was 483.89 ± 10.18 per 1,000 persons. That figure is somewhat lower for men than it is for women. The highest morbidity level was observed in the following age groups: under 1 year, 966.81 ± 13.85 ; 1-3 years, 882.98 ± 7.30 ; 30-39 years, 613.98 ± 12.10 per 1,000 persons.

The results presented reflect the morbidity level upon continuous observation without differentiating the regions into experimental and conventional categories. We found it necessary to analyze the morbidity level under experimental conditions in order to achieve the purpose of our study (table).

Level of Morbidity Among Rural Population of Experimental SVU [not further identified] of Romaneshta in Strashenskiy Rayon As Determined by Data of Patient Visits as a Function of Age and Sex (per 1,000 persons)

Age, in years	Sex		
	Men	Women	Both Sexes
Under 1 year	881.0 \pm 7.73	854.0 \pm 6.95	869.0 \pm 7.25
1-3	748.0 \pm 6.39	762.0 \pm 5.54	755.0 \pm 6.03
3-7	1090.0 \pm 4.82	1310.0 \pm 2.13	1200.0 \pm 2.44
7-14	601.0 \pm 7.53	664.0 \pm 5.23	635.0 \pm 6.07
15-17	277.0 \pm 9.82	581.0 \pm 6.10	417 \pm 7.19
18-19	236.0 \pm 9.86	387.0 \pm 6.87	316.0 \pm 8.41
20-24	386.0 \pm 9.56	542.0 \pm 4.66	468.0 \pm 6.78
25-29	742.0 \pm 6.42	782.0 \pm 4.12	763.0 \pm 6.10
30-39	850.0 \pm 5.93	1040.0 \pm 1.89	949.0 \pm 2.15
40-49	630.0 \pm 6.36	1160.0 \pm 2.01	875.0 \pm 3.98
50-59	936.0 \pm 3.01	1070.0 \pm 1.77	1010.0 \pm 2.15
60-69	937.0 \pm 2.11	791.0 \pm 2.47	851.0 \pm 2.39
70 or older	581.0 \pm 4.67	474.0 \pm 5.69	525.0 \pm 4.69
Totals	660.0 \pm 5.16	866.0 \pm 4.27	796.0 \pm 4.98

The results given in the table show that the morbidity level is higher under experimental conditions and came to 796.0 ± 4.98 per 1,000 population in 1982, with the rate for men (660.0 ± 5.16) significantly higher than for women (866.0 ± 4.27). The morbidity per 1,000 persons was higher in the following age groups: 3-7 years (1200.0 ± 2.44), 50-59 years (1010.0 ± 2.15), 30-39 years (949.0 ± 2.15), 40-49 years (875.0 ± 3.98), 60-69 years (851.0 ± 2.39). It was lower in the remaining age groups.

In connection with the better identification of illnesses under experimental conditions, the morbidity rate for 1980 was 1.4 times higher than the 1982 level. During that period the frequency of patient visits to treatment-and-prevention institutions among rural population by age group increased by a factor of 1.3 for the group under 1 year, by 1.4 for the 1-3 year group; by 3.9 for the 3-7 group; by 0.9 for the 7-14 group; by 2.9 for the 15-17 group; by 1.8 for the 18-19 group; by 2.5 for the 20-24 group; by 2.4 for the 25-29 group; by 1.5 for the 30-39 group; by 1.5 for the 40-49 year group; by 1.6 for the 50-59 group; by 1.7 for the 60-69 year group; and by 1.7 for the group 70 years or older.

At the same time, there still was a high percentage of persons who did not seek medical assistance during the year at outpatient-polyclinic institutions and therefore were not examined by physician specialists. The average figure for all ages in that contingent was 22.1%.

As a function of age, the percentage of persons who did not seek medical assistance at the outpatient-polyclinic institutions in 1982 decreased by a factor of 1.2 by comparison with 1980. Those reductions were as follows: by a factor of 2.2 for the 1-3 year group; by 1.2 for the 3-5 group; by 0.7 for the 7-14 group; by 1.5 for the 15-17 year group; by 1.4 for the 18-19 group; by 1.1 for the 20-24 year group; by 2.3 for the 25-29 group; by 1.6 for the 30-39 year old group; by 1.04 for the 40-49 group; by 1.9 for the 50-59 group; by 1.5 for the 60-69 group; and by 1.2 for the 70 or older group. At the same time, there were no children under the age of one who had not been at medical institutions.

Under the experimental conditions, the principal reason for visits to medical facilities was found to be pathology involving the respiratory organs, trauma and poisonings, and digestive tract diseases.

The results of our study showed that children aged 15 or under are afflicted with respiratory organ diseases 3.2 times more frequently than persons aged 16-70 years. Respiratory organ diseases accounted for the greatest percentage (53.13%) of all pathology recorded for the children 1-2 years old. In terms of overall morbidity, respiratory organ diseases represent the No. 1 disease among individuals 20-24 years old or younger.

Digestive tract disease accounts for the second highest incidence of disease among individuals 15-24 years old, behind respiratory organ diseases. Digestive tract diseases occupy first place in the morbidity picture for the age group 25-29. The greatest percentage of digestive organ diseases was found in the 50-59 group. The results of our analysis showed that there is no significant difference in the frequency of visits by men and women to medical facilities for this class of disease ($p > 0.05$).

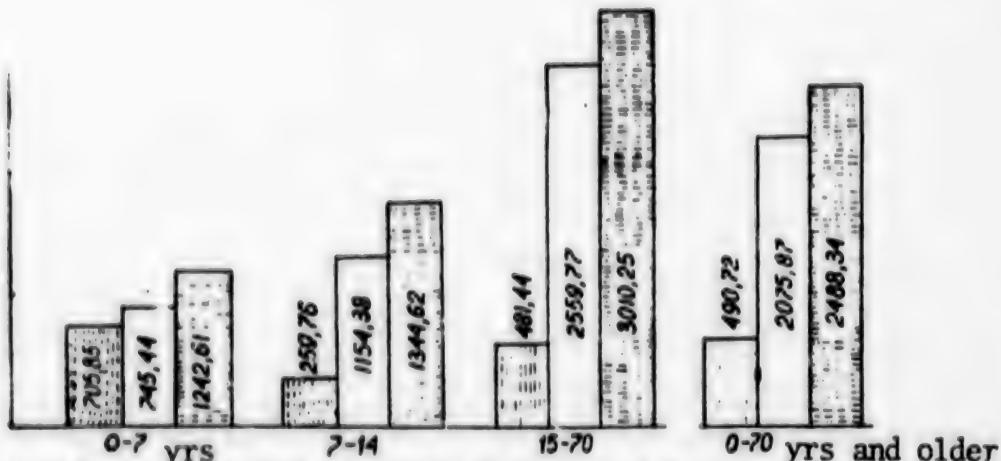
Trauma and poisonings account for the highest levels of morbidity in the 7-14, 18-19, and 25-29 age groups and occupy second place in the overall morbidity structure of the population. Trauma and poisonings are recorded more frequently for men than for women. The figure is higher for men by a factor of 2.8 for the 25-29 age group, 1.8 for the 30-39 age group, 1.7 for the 40-49 age group, and 1.6 for the 50-59 age group.

Thus, our analysis of the morbidity rate based on the frequency of the rural residents' visits to medical facilities has identified predominant diseases at various stages. These data, in combination with other health care figures, make it possible to forecast the optimal forms of organizing rehabilitation, medical, and sanatorium-health resort services for rural residents in the context of universal mass health screening.

In order to find the true level and structure of the overall level of rural morbidity, a study must be made of these indices and of the data obtained from comprehensive medical examinations. The results of our study have shown that there are significant differences in the levels of rural resident morbidity as reflected by the data on the frequency of visits to medical facilities and comprehensive medical examinations (figure). The level of morbidity according to the comprehensive medical examination data was 4.1 times higher than the level reflected by the frequency of medical visits.

In our view, the observed differences are due the following principal reasons: the low frequency of visits to outpatient-polyclinic institutions; the shortage of physicians and middle-level medical personnel at rural outpatient-polyclinic institutions; the failure of physicians in terms of early detection of disease; the absence of an appropriate material-and-technical base at rural health care institutions; poor coverage of rural residents in terms of preventive examinations and universal mass health screening; poor sanitation; lack of interest on the part of local soviets of people's deputies and directors of kolkhozes, sovkhozes, and inter-farm organizations in maintaining and safeguarding the health of their own workers; and the absence of a scientifically substantiated system of universal mass health screening for rural workers.

The data that describe the differences between the morbidity levels of men and women in relation to their age are considerable interest since they are important to the organization of rehabilitation, medical and sanatorium



Level of rural population morbidity according to data on the frequency of visits to medical facilities and a comprehensive medical examination by age group (per 1,000 persons); first column—from data on frequency of medical facility visits; second column—from comprehensive medical examination data; third column—from both frequency of visits and the comprehensive medical examination.

services and the implementation of universal mass health screening. Diseases of the ear and appendix, for example, are found 3.5 times more frequently in male children 1 year old or younger. In female children aged 1-3 years, acute respiratory illnesses are encountered 1.6 times more frequently, and eye and adnexa oculi diseases, 1.8 times more frequently. Males aged 3-7 are afflicted with infectious and parasitic diseases 3.6 times more frequently. Males in the 7-14 group are afflicted with blood and hemopoietic organ diseases 1.7 times more frequently and with urogenital diseases 1.4 times more frequently.

Females in the 15-17 age group are afflicted with infectious and parasitic diseases 3.5 times more frequently. Males in that age group are afflicted 2.6 times more frequently with skin and subcutaneous diseases. The level of neurotic disorders in the 20-24 age group was 10.1 times greater among women; chronic diseases of the tonsils and adenoids were encountered 3.1 times more frequently among women of that group. In the 25-29 age group, neurotic disorders were found 15.1 times more frequently among women; gastritis and duodenitis were identified 1.9 times more frequently; and diseases of the veins, lymph vessels, and other diseases of the circulatory system were found 4 times more frequently.

Neurotic conditions were encountered 5.0 times more frequently among women in the next age group (30-39). Men in that age group were afflicted 3.4 times more frequently with dorsopathy. Neurasthenia was recorded 7.2 times more frequently among women in the 40-49 age group, and chronic diseases of the tonsils and adenoids were encountered 6.2 times more frequently. During that period of life men are afflicted with chronic obturation of the lungs 7.4 times more frequently and with chronic bronchitis 9.5 times more frequently.

Malignant tumors were found 3.1 times more frequently among the older male groups, with abdominal hernias encountered in those groups 5.9 times more frequently.

The data of expert evaluation of the remaining nosological forms of illnesses indicate that there are no significant differences among men and women in the various age groups. An analysis of overall morbidity is of considerable importance for a full description of the morbidity picture.

Thus, an analysis of our study results indicates the three most frequently encountered diseases in order of prevalence are digestive tract diseases—including stomatological pathology—diseases of the nervous system and sensory organs, and lastly, diseases of the respiratory organs. The cumulative morbidity rate for the rural population was 2,488.34 per 1,000 inhabitants, including 2,358.00 for the men and 2,593.56 for the women. There are significant differences in the levels of morbidity distribution as reflected by data on the frequency of visits to medical facilities and comprehensive medical examination with respect to age, sex, and categories of diseases.

The level of morbidity we established from the data on frequency of patient visits and comprehensive medical examinations constitutes an objective basis for finding the differential need of the rural population for specialized outpatient-polyclinic, hospital, and sanatorium-health resort services, universal mass health screening and rehabilitation of patients, as well as a basis for designing a scientifically substantiated system for the dynamic observation of the rural population's health in the context of the intensive chemicalization of agriculture and annual mass health screening of rural residents.

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UDC 616-082].003.1(47+57)

Problems in Developing Fee-Based Medical Care for the Public

18400286 Moscow SOVETSKAYA
ZDRAVOKHRANENIYE in Russian No 11, Nov 88
(manuscript received 4 Apr 88) pp 9-12

[Article by V. V. Grishin and G. Yu. Shvyrkov, USSR Ministry of Health, Institute of Economic Problems in the Integrated Development of the National Economy, Moscow]

[Text] The "Basic Guidelines for Developing Public Health Safeguards and Restructuring Health Care in the USSR During the 12th Five-Year-Plan and for the Period up to the Year 2000" stipulates increasing the amount of fee-based medical services fivefold by the year 2000 and significantly strengthening the material and technical base of cost-accounting health care institutions.

Until recently, not enough attention was devoted to fee-based care in the health care sector. Between 1970 and 1980, only 13 cost-accounting consultation-and-diagnostic stomatological polyclinics were reorganized in the country, and not a single fee-based polyclinic was opened. The network of dental prosthesis departments and offices developed slowly. In the 11th and the current five-year-plans, development of the network of cost-accounting institutions and their subdivisions accelerated somewhat.

By the beginning of 1988, a total of 184 cost-accounting treatment-and-prevention institutions providing the public with fee-based medical services (55 stomatological and 129 consultation-and-diagnostic and physiotherapy polyclinics, cosmetology clinics, etc.) were functioning. In addition, fee-based dental prosthesis and stomatological care was being provided by about 6,800 cost-accounting departments and offices that are components of budgetary health care institutions. The network

of cost-accounting treatment-and-prevention institutions is located throughout the country's territory in a very uneven manner. Those institutions are primarily located in the largest cities and the capitals of the union republics. There are 20 in Moscow. In a number of union republics, no such institutions have as yet been organized. In all, there are about 120,000 posts for medical and other personnel in the cost-accounting treatment-and-prevention institutions and health care subdivisions. About 21 percent of those posts are for physicians.

In the cost-accounting polyclinics, for a moderate fee and regardless of place of residence, the public receives highly skilled medical care both of the general and narrowly specialized types: hematology, allergiology, gastroenterology, sexual pathology, acupuncture therapy, cosmetology, etc. The treatment of patients with chronic alcoholism, including confidential treatment, and assistance to those desiring to quit smoking are expanding. Modern methods of instrument-and-laboratory diagnosis and different types of complex dental prostheses are being used.

Fee-based services, however, currently account for less than 1 percent of the total volume of medical care from the standpoint of number of visits, and they do not meet the public's needs. For this reason, the fear that fee-based health care services will hinder free medical care and thereby replace it is not well-founded, not even in the distant future.

In monetary terms, fee-based medical services in 1986 amounted to almost 275 million rubles, or 1.31 rubles per adult inhabitant. In 1987, the amount of fee-based medical care increased by 48.6 percent and surpassed 400 million rubles, which amounted to 1.94 rubles per adult inhabitant. Despite the substantial increase in the amount of this type of medical care, the gap between the levels of public expenditures has been maintained throughout the union republics.

It should be noted that treatment-and-prevention institutions of other ministries and departments have provided medical services to the public in the amount of about 30 million rubles, or 7.3 percent of the total amount of fee-based medical care in monetary terms. The main portion of public expenditures currently goes for dental prostheses (in some republics as high as 80 percent). In 1986, some 7.5 million persons received dental prosthesis services, which averaged 26.5 individuals per 1,000 population throughout the country. For the adult population, this indicator amounts to 35.6 per 1,000 (from 13-24 per 1,000 in the AzSSR, TuSSR, UzSSR, and TaSSR to 47-58 per 1,000 in the Baltic republics).

In 1986 the Moscow Institute of Economic Problems in the Integrated Development of the National Economy studied the activity of cost-accounting treatment institutions in the capital. The study revealed a number of serious problems in the organization of this type of

medical care. Moscow's fee-based medical services to the public account for 3.7 percent of all such services in the country. In fact, the figure is higher since fee-based medical services are also provided by medical military commissions, sanitary and epidemiological stations, and certain other institutions. Visits to cost-accounting outpatient polyclinic institutions represent a substantial percentage of the total number of visits to territorial polyclinics—about 4 percent.

The visit time norms used in cost-accounting consultation-and-diagnostic polyclinics do not conform to modern requirements set for the quality of medical care. In practice, physicians at cost-accounting polyclinics spend one and a half to two times as much time with a patient than is stipulated by the norms. This is mainly because 50 percent of the patients are presenting for the first time, and examining them requires considerably more time than does examining a returning patient.

The shortage of work space is a serious problem for Moscow's cost-accounting polyclinics. Most cannot set up the proper conditions for visitors and personnel or for placement of medical equipment.

The profit margins of cost-accounting polyclinics represent one of the main problems. The existing rates do not enable them to recover their expenses fully, they lag considerably behind in terms of the new types of services that are constantly emerging, and they give rise to an imbalance in the economic activity of polyclinics.

Over a 10-year period (from 1976 through 1985), the volume of fee-based services that were provided by cost-accounting treatment institutions in Moscow increased 1.3-fold, with the profits of the consultation-and-diagnostic polyclinics growing 1.5-fold and those of the stomatological polyclinics falling by a factor of almost 4.5.

Naturally, this situation has had an effect on profitability. In the period of the study, general profile polyclinics received 1.23 rubles per ruble spent, whereas stomatological polyclinics received only 1.06 rubles. The latter's profitability level continually declined, with some of the polyclinics showing a loss. One reason for this situation is the absence of changes in rates for services at stomatological polyclinics despite a change in the prices of medical supplies, the cost of which constitutes a very substantial percentage in the expenditure structure. If medical supplies account for only 5.4 percent of outlays at consultation-and-diagnostic polyclinics, they account for 47.3 percent at stomatological polyclinics.

In general, analysis of the economic activity of fee-based polyclinics shows that rates for services at cost-accounting treatment institutions do not support the implementation of the principles of cost-accounting and do not meet the needs of the segment of the public capable of paying. Thus, only one of every six persons desiring to obtain a given type of service is served at

stomatological polyclinics each visiting day. In consultation-and-diagnostic polyclinics, the waiting time ranges from one week to two months. At the same time, cost-accounting polyclinics are considerably overloaded. The number of patients actually seen by physicians is 2- to 3.5-fold higher than the polyclinics' certified capacity. An overload is also evident in the ancillary services (laboratories) of consultation-and-diagnostic polyclinics, where only one out of two persons desiring an examination is accepted per shift.

During the 10th and 11th five-year-plans, 35.2 percent of the requests for medical assistance in the consultation-and-diagnostic polyclinics were unsatisfied. Because of inadequate capacity, about 4 million persons needing different types of medical care were not seen by physicians. The existing rates at which fee-based medical services to the public are developing are inadequate to meet such a substantial demand. During the 11th Five-Year-Plan, the number of visits to cost-accounting consultation-and-diagnostic polyclinics increased by 14 percent and to stomatological polyclinics, by 8 percent.

The slow pace at which the system of cost-accounting treatment institutions is being developed and the substantial, ever-increasing load placed on this network by those traveling from other localities are facilitating the build-up of an unsatisfied demand on the part of the population segment capable of paying for such services. This is also confirmed by the results of a survey conducted in Moscow. The average cost of a visit to any type of fee-based polyclinic, in the estimation of the patients themselves, could be nearly triple the existing average rate, on the condition that patients' needs were met fully.

The average projective rate (obtained during the survey and tied to the condition that the needs for a level of medical care be met completely) for services at consultation-and-diagnostic polyclinics, based on visitors' estimates, was 13 rubles. For stomatological polyclinics, it was approximately 13.5 rubles. Such a substantial discrepancy between the existing and the projective rates not only indicates the public's willingness to pay for services provided by cost-accounting polyclinics with higher rates, but also directly reflects effective demand people and the feasibility of assessing it.

In cost terms, about 50,000 rubles' worth of services daily are currently being provided to the public by Moscow's cost-accounting polyclinics. Based on estimates of effective demand, the volume of medical services provided by these fee-based polyclinics ranges from 300,000 to 900,000 rubles per day. Thus, only 17 percent of the minimum estimated amount of the effective demand is being satisfied.

Most (67 percent) indicated that expenditures for treatment are not a burden on the family budget. Slightly more than 77 percent of those surveyed indicated that there is a need to set up an emergency medical service and agreed to pay for this type of service at a higher rate.

Yet another point in favor of a possible increase in rates for services provided by cost-accounting polyclinics is the distribution of visitors based on average per capita yearly incomes. Individuals with an income of no more than 85 rubles per month, for example, account for 21.3 percent of visitors, whereas those earning between 85 and 150 rubles per month account for 57.2 percent. Thus, 78.5 percent of visitors to cost-accounting polyclinics belong to low- and middle-income groups. This fact reflects the accessibility of the services of cost-accounting consultation-and-diagnostic and stomatological polyclinics for individuals with different income levels.

According to those surveyed, the main reason the public seeks medical care at cost-accounting polyclinics of any profile is the higher qualifications of the physicians in these polyclinics (56.6 percent). The other reasons given after this were greater attentiveness to needs on the part of the medical personnel (38.5 percent), the lack of the appropriate specialists in rayon polyclinics (20.9 percent) or of necessary medical equipment (19.2 percent), and higher-quality medical supplies and medications (18.4 percent). For stomatological polyclinics, the last reason ranks third (26.9 percent).

With regard to the question of whether the cost-accounting polyclinics meet current needs, 71.8 percent of visitors responded positively, 5.5 percent responded negatively, and 22.7 percent declined to answer.

A study of the activity of cost-accounting health care institutions in a number of regions of the country (including Moscow) showed that the development of fee-based medical care is being held back by the weak material and technical base of most cost-accounting institutions, many of which have small capacities, are in poorly adapted locations, do not have modern diagnostic equipment, or are inadequately equipped with medical instruments and supplies. Many institutions lack the conditions for comprehensively conducting examinations and treatments.

Such forms of fee-based medical services as at-home laboratory and x-ray studies, ECGs, injections, massages, geriatric nursing, nursing for invalids and chronically ill persons, as well as physical therapy, acupuncture therapy, confidential treatment for alcoholics, and artificial abortions are developing slowly.

The problems of improving price setting and the mechanism of the financial management of the activity of cost-accounting polyclinics have not been addressed in a proper manner for many years. Rates for fee-based medical service do not enable full recovery of actual outlays, and they do not make allowances for increases in health care workers' wages, the use of new, expensive diagnostic equipment, or changes in prices for medical supplies.

The existing mechanism of the financial management of fee-based medical care sharply restricts the independence of cost-accounting health care institutions in their use of labor, financial, and physical resources. The profit of profit-making cost-accounting institutions is confiscated for the budget, which makes it impossible to create funds to strengthen their material and technical base, social development, or material incentives for their workers.

The existing system of paying for personnel's labor does not make allowances for the ever-increasing role of the principle of material incentives and does not stimulate an increase in quality or volume of medical care.

Cases of poor economic justification of decisions, incorrect calculation of rates and prices for individual types of services, and poorly targeted monetary outlays are common because of the inadequate level of the economic training of the directors and specialists of cost-accounting treatment institutions. There is no system of economic training and retraining for workers at these institutions.

In general, the sphere of fee-based medical services is inert and slow to react to demand. The changes that are occurring do not meet the public's needs or their rapidly increasing requests.

The USSR Ministry of Health and its local organs are working to develop a network of cost-accounting institutions and corresponding subdivisions at budget-funded health care institutions, strengthen their material and technical base, and increase the amount of fee-based medical services both from the standpoint of mass traditional types of assistance to the public and from the standpoint of organizing new types.

The organization of new types and forms of medical care should be singled out among the problems of the further development of fee-based medical services in the country. The organization of the following types of services is possible at the present time:

- Fee-based consultation with professorial and teaching personnel and highly-skilled specialists at budget-funded hospitals and polyclinics and at clinics at higher educational institutions and scientific research institutes
- Hospital treatment (requiring full or partial payment) of chronically ill patients
- Fee-based provision of lodging to retirees coming for consultation and to the persons accompanying them, and outpatient treatment for these patients
- Expansion of the range of fee-based outpatient-polyclinic care that is provided in resort areas and at large tourism centers
- An office to care for patients at home, services of the Medical Service (the at-home provision of different types of therapeutic and health improvement procedures, laboratory and diagnostic studies, etc.)

- The renting of individual types of medical technology
- Mobile types of medical care, particularly in rural areas
- Fee-based consultation-and-diagnostic and health improvement centers, including those organized on the basis of treatment-and-prevention institutions and enterprises of various ministries and departments
- Consultation services provided by "Brak i semya" [Marriage and Family] as well as consultations related to sexual pathology and psychotherapy, treatment of speech and hearing disorders, etc.
- Signing of agreements with enterprises and organizations for various types of supplementary treatment-and-prevention measures

The public needs special types of medical care provided on an emergency basis at night (it is advisable to provide these services at higher prices) and medical information services (consultations, for example, on healthy life-style and prevention—including telephone advice—and selection of medical reference literature, etc.).

The main reason for the inertia of health care organs and institutions in the development of fee-based medical services for which there is a demand is their lack of economic incentive. For this reason, altering the distribution of profits produced by institutions and subdivisions is one of the first steps that needs to be taken in restructuring the system of fee-based medical services.

The capital from consumers using fee-based medical services can serve as an additional source for the outlays needed for the development of health care. In addition, full cost-accounting assumes a fiscal relationship with the government. In our view, it is advisable that the main portion of the profits earned by institutions providing fee-based medical services to the public be left at the disposal of the institutions, that only a small portion of the earned capital be transferred to the budget, and, after a stable norm has been established for withholding part of the profit for the local budget, that this capital be directed exclusively toward medical needs. The right to dispose of it should be given to the appropriate higher-ranking health care organ. This will make it possible not only to interest health care organs in developing this service, but also to obtain a rather sizable financial supplement toward the development of the material and technical base of budget-funded health care.

The profit left at the disposal of the cost-accounting institutions should be directed toward providing material incentives to personnel, acquiring equipment and hardware, conducting capital repair, and paying off debts for construction and their relative share of residential construction, etc.

The economic and organizational problems in developing fee-based medical care in the country have more to do with improving quality and conditions, introducing progressive forms and new types of services, and

improving the mechanism of managing the activity of the appropriate health care institutions than with increasing the volume of fee-based medical care.

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UDC 616-006-089.168

Results of a Census of Oncology Patients Who Were Treated in a Number of Permanent Medical Facilities in Leningrad in 1982

18400294 Leningrad VOPROSY ONKOLOGII in Russian Vol 34 No 10, Oct 88 (manuscript received 12 Jul 88) pp 1237-1245

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[Text] The conduct of the large-scale experiment called for in the "Basic Guidelines for the Development of Public Health Protection and the Restructuring of Health Care in the USSR in the 12th Five Year Plan and for the Period Up to the Year 2000" to improve the economic mechanism of health care management in Leningrad has led to the need to collect data and to analyze the survival rate of oncology patients in various types of permanent medical facilities. For this purpose, the first stage of research involves a study of morbidity due to malignant neoplasms among the resident of Leningrad.

Between 1970 and 1986, the average annual increase in oncological morbidity was 1.4%. It should be noted that after a slowing of the rates of growth of oncological morbidity in the second half of the 1970s, the average annual rates of growth of morbidity due to malignant neoplasms among the Leningrad population increased in the 1980s. The gross indices of morbidity grew to 321 per 100,000 from 263.4, whereas the standard indices (the world standard) went from 227.9 per 100,000 from 206.4 (with an average annual growth of 0.7%). An analysis showed that the high level of gross indices of oncological morbidity is associated with the relatively large percentage of individuals of middle age in the structure of the city population; 50% of the growth in morbidity among the Leningrad population is associated with the continuing aging of the population.

Between 1970 and 1986, the number of oncology patients almost doubled, from 33,400 to 62,200. The frequency index of the prevalence of malignant neoplasms grew, on average, by 3%. It should be noted that, based on the city's population growth, the average annual growth of the absolute number of oncology patients is quite high, at 5.4%. If the rate of growth of oncology patients continues, the absolute number will exceed 70,000 by 1990.

Data have been presented for the first time on the dynamics of oncological morbidity for virtually all types of malignant tumors in men and women of Leningrad; they accounted for 97.2% of all malignant neoplasms in men and 97.4% in women. We evaluated the basic patterns of the dynamics of hormone-dependent tumors in women in materials pertaining to an earlier period.⁴

The basic forms of tumors in men in Leningrad in 1986 were lung cancer (82.3 per 100,000), stomach cancer (52.9 per 100,000), cancer of the oral cavity and throat (19.5 per 100,000), cancer of the large intestine (19.0 per 100,000), rectal cancer (17.9 per 100,000), skin cancer (15.3 per 100,000), cancer of lymphatic and hemopoietic tissue (13.0 per 100,000), prostate cancer (12.5 per 100,000), esophageal cancer (12.2 per 100,000), and cancer of the urinary bladder (11.6 per 100,000). The highest rates of growth were recorded for cancer of the large intestine and cancer of the oral cavity and throat, and the morbidity figure for cancer of pancreas in men grew substantially (to 11.0 per 100,000 from 8.2), although its ranking did not change (11th place). The next group of neoplasms close in terms of morbidity figures includes laryngeal cancer (9.1 per 100,000) and neoplasms of the kidneys (5.9 per 100,000) and liver (5.6 per 100,000).

The principal forms of malignant tumors among women in Leningrad include breast cancer (65.2 per 100,000), stomach cancer (50.7 per 100,000), cancer of the large intestine (30.3 per 100,000), rectal cancer (20.6 per 100,000), skin cancer (19.8 per 100,000), lung cancer (17.7 per 100,000), cancer of the corpus uteri (17.0 per 100,000), cervical cancer (14.3 per 100,000), and pancreatic cancer (12.8 per 100,000). In this group of neoplasms, the highest average annual rates of growth belong to tumors of the breast (5.2%), the pancreas (3.6%), the corpus uteri (3.4%), and the large intestine (2.9%). Next in the structure of oncological morbidity among women in Leningrad are malignant neoplasms of lymphatic and hemopoietic tissue (12.1 per 100,000), the esophagus (7.9 per 100,000), the kidneys (6.1 per 100,000), the thyroid gland (4.8 per 100,000), the gallbladder (4.3 per 100,000), the liver (4.1 per 100,000), and the brain and peripheral nervous system (3.8 per 100,000). It is important to note that in this group of neoplasms, the highest rates of growth of morbidity figures have been noted for tumors of the brain and peripheral nervous system, as well as the thyroid gland.

On the basis of a study of the dynamics of morbidity due to malignant neoplasms among residents of Leningrad and of the information file on primary registration of oncology patients, as well as on the basis of an analysis of patient histories, we have developed a special program for comparative evaluation of the long-term outcomes of treatment of oncological patients in various kinds of permanent medical facilities.

Leningrad has 1,340 special oncology beds, of which 380 are allotted for radiology patients and 40 for children. The figure for oncology beds for the Leningrad population is considerably lower than the figure for the entire

country (93 per 1,000 Leningrad residents, as opposed to 102.7 for the USSR).⁶ Assigning 120 beds to the oncology department in hospital No 12 does not solve the problem of a bed shortage. It should be noted that the operational bed plan is being met by more than 100% in the oncology facilities of the city. In addition, some of the beds are not used for their intended purpose. The length of stay of a patient in a bed in the 1980s did not change substantially and is about 30 days in various types of special oncology facilities.

In the overwhelming majority of cases, treatment of the oncology patient at present consists of combined use of surgical, irradiation, and drug therapy techniques.⁷ Because of the shortage of oncology beds, nearly 40% of the patients are treated in hospitals of the general treatment-and-prevention system, which, as a rule, does not have the necessary diagnostic or treatment equipment, or special drugs for complex or combined therapy for malignant tumors.⁸ Our analysis of the information on patients with first-time diagnosis of malignant neoplasm shows that the composition of oncology patients who are hospitalized in facilities of the general treatment-and-prevention system is not uniform. For example, in Leningrad in 1986, nononcology medical facilities treated 86.4% of the stomach cancer patients, 57.3% of rectal cancer patients, 47.3% of lung cancer patients, and 29.3% of the breast cancer patients. Some of these patients go to emergency facilities for complications associated with a malignant tumor (circulation, peritonitis, or perforation, for example). This contingent of patients is given whatever emergency assistance is needed in connection with the clinical picture that exists when they come into the facility. By and large, these patients have a long neglected problem, which, in many cases, does not preclude the possible use of radiation or drug therapy to produce remission. In facilities of the general treatment-and-prevention system, these possibilities are virtually nonexistent because of the reasons given above. A second group of patients (primarily with visceral tumors) go to hospitals of the general treatment-and-prevention system on a regular basis for surgery.

In evaluating survival rate in this study, we limited ourselves to patients with the principal sites of malignant neoplasms (stomach, rectum, lungs, breast, cervix and corpus uteri, and ovaries).

In connection with the need to study the five-year survival rate of this group of patients, the year 1982 was established as the base year for collecting the initial information.* When there were not enough observations of certain sites, we went to data on oncology patients with first-time diagnosis from previous years for representative data.

The hospital facilities in which the oncology patients were treated were arbitrarily divided into three types. The first two types consisted of permanent specialized oncology facilities of the Scientific Research Institute of

Oncology imeni Prof. N. N. Petrov of the USSR Ministry of Health (SRI Oncology) and of the Leningrad City Oncology Clinic. Medical institute clinics and the permanent facilities of medical units and city general hospitals made up the third group of treatment facilities. Overall, more than 70 Leningrad institutions, which treat the overwhelming majority of oncology patients, are represented in the study.

In stage I of the research, staff members of the scientific and clinical subdivisions of the SRI Oncology conducted a

census of oncology patients and copied data about the patients from their histories in the archives of the medical institutions.^{**} Tables 1 and 2 present data on 6,238 patients with principal sites of malignant neoplasms (SRI Oncology, 2,272 patients; Leningrad City Oncology Clinic, 1,845; other permanent facilities, 2,121). A special search enabled us to identify the fate of 5,930 individuals, or 95.2% (SRI Oncology, 97.9%; Leningrad City Oncology Clinic, 94%; and the other facilities, 93%).

Table 1. Distribution of Malignant Neoplasm Patients by Leningrad Permanent Facility

Treatment facility	Total number of patients	Morphological confirmation of diagnosis (in %)
SRI Oncology imeni N. N. Petrov	2,272	94.6
Leningrad City Oncology Clinic	1,845	76.5
Nononcological Permanent Facilities	2,121	44.7
—1st Leningrad Medical Institute	408	54.2
—Hospital No 16	344	24.4
—Military Medical Academy imeni S. M. Kirov	283	61.8
—Hospital No 1	191	25.6
—Hospital No 26	164	40.8
—Leningrad Health and Hygiene Medical Institute	161	68.3
—Medical Unit No 18	94	58.5
Other hospital facilities	476	39.8
Totals	6,238	72.2

Table 2. Distribution of Patient Treated in Various Permanent Facilities of Leningrad, by Nosological Form of Oncology

Tumor site (MKB-9)	SRI Oncology		Len. Oncology Clinic		Other facilities		Totals	
	Total	Morphologically confirmed diagnosis	Total	Morphologically confirmed diagnosis	Total	Morphologically confirmed diagnosis	Total	Morphologically confirmed diagnosis
	Abs. No.	%	Abs. No.	%	Abs. No.	%	Abs. No.	%
Stomach (151)	292	82.2	257	63.8	736	39.7	1,285	54.2
Rectum (154)	281	100.0	186	85.5	331	44.1	789	73.4
Lungs (162)	329	96.1	184	58.2	541	23.3	1,054	52.1
Breast (174)	547	96.2	553	69.6	288	78.8	1,388	82.0
Cervix (180)	236	98.7	330	98.2	43	67.4	609	96.2
Corpus uteri (182)	332	96.1	243	86.4	72	87.5	647	96.1
Ovaries (183)	255	92.9	92	57.6	110	60.9	457	78.1

The figures for morphological verification of tumors in the clinics of the SRI Oncology fluctuate from 82%, with stomach tumors, to 100%, with rectal tumors. Those levels are somewhat lower in the Leningrad City Oncology Clinic. The existing levels of the figures for individual sites in the permanent facilities of the general treatment-and-prevention system cannot be considered

satisfactory. For example, morphological verification was effected in only 23.3% for lung tumors, in 39.7% for stomach tumors, and in 44.1% for rectal tumors. Interestingly, the group of treatment-and-prevention facilities had high levels for morphological verification of tumors of the breast (78.8%) and the corpus uteri (87.5%). Among the permanent nononcological facilities that treat oncology patients (see Table 1), the highest level of

morphological confirmation of malignant tumor diagnosis belongs to the clinics of the Leningrad Health and Hygiene Medical Institute (68.3%) and the Military Medical Academy imeni S. M. Kirov (61.8%), as well as to Medical Unit No 18 (58.5%). In other hospitals, this figure fluctuates from 25.6% to 40%.

Information on incidence is extremely important for evaluating the outcomes of treatment. Table 3 presents

such data for the three groups of facilities. Noteworthy is the high percentage of patients who were treated in facilities of the general treatment-and-prevention system and in whom the stage of the disease process was generally not determined. A specific example involves the absence of data on stage of illness in more than 50% of patients with tumors of the corpus uteri; that figure is 29% for lung tumors and 25% for cervical tumors.

Table 3. Distribution of Patients by Stage of Disease in Leningrad Permanent Facilities

Treatment facility	Total no. of patients	Stage of disease (% of total)				
		I	II	III	IV	Stage not indicated
Stomach cancer (151)						
SRI Oncology	292	3.1	8.6	49.7	36.6	2.0
Leningrad City Oncology Clinic	2,507	0.8	7.7	33.5	43.8	14.2
Other permanent facilities	736	1.4	4.7	20.5	51.9	21.5
Totals	1,285	1.6	6.2	29.7	46.8	15.7
Rectal cancer (154)						
SRI Oncology	281	4.6	18.5	58.4	17.1	1.4
Leningrad City Oncology Clinic	186	4.2	17.2	53.1	21.9	3.6
Other permanent facilities	331	3.6	18.4	22.1	37.2	18.7
Totals	798	4.1	18.2	42.2	26.5	9.0
Lung cancer (162)						
SRI Oncology	329	13.9	31.2	36.2	14.8	3.9
Leningrad City Oncology Clinic	184	2.7	13.8	31.4	20.7	31.4
Other permanent facilities	541	0.5	9.8	18.1	42.6	29.0
Totals	1,054	5.0	17.1	25.9	30.3	21.7
Breast cancer (174)						
SRI Oncology	547	21.7	36.7	37.6	2.6	1.4
Leningrad City Oncology Clinic	553	7.8	51.3	26.3	3.8	10.8
Other permanent facilities	288	9.2	47.4	20.1	9.6	14.7
Totals	1,388	13.3	44.7	29.5	4.5	8.0
Cervical cancer (180)						
SRI Oncology	236	38.3	36.2	22.5	2.1	0.9
Leningrad City Oncology Clinic	330	21.9	40.6	33.0	3.0	0.9
Other permanent facilities	43	4.6	14.0	20.9	34.9	25.6
Totals	609	27.0	37.0	28.2	5.2	2.6
Corpus uteri cancer (182)						
SRI Oncology	332	72.6	14.5	6.0	4.2	2.7

Table 3. Distribution of Patients by Stage of Disease in Leningrad Permanent Facilities

Treatment facility	Total no. of patients	Stage of disease (% of total)				
		I	II	III	IV	Stage not indicated
Leningrad City Oncology Clinic	243	13.4	71.2	7.7	5.7	2.0
Other permanent facilities	72	6.8	20.3	10.8	10.8	51.3
Totals	647	42.8	36.5	7.2	5.5	8.0
Ovarian cancer (183)						
SRI Oncology	255	13.7	6.7	5.9	73.3	0.4
Leningrad City Oncology Clinic	92	13.8	4.3	37.2	36.2	8.5
Other permanent facilities	110	10.4	16.5	17.4	40.9	14.8
Totals	457	12.9	8.6	15.1	57.8	5.6

One of the fundamental indicators of the effect of treatment is the survival rate of oncology patients. At present, an attempt is being made for the first time to evaluate the outcomes of treatment among the basic groups of malignant tumors in a large city. In connection with the fact that in this study an analysis is being made of the basic patterns of the quality of treatment on the basis of selected material,*** the method of observing survival rate underlies the evaluation.¹ The analysis of the findings is preliminary and needs further in-depth critical analysis based on a complex evaluation of a number of factors. Some 40-50% of oncology patients are treated in treatment-and-prevention facilities; but the low percentage of morphological verification of diagnosis and the absence of accurate data on the stage of the disease lead to a situation in which reliable five-year outcomes are produced in not nearly all the patients who receive so-called radical treatment. Indicating this is the survival rate observed for individual tumor sites, which, depending on the method of treatment and the stage of the disease, does not always go into the traditional concept of long-term outcomes. In individual cases, these figures may be explained by the small number of observations that went into the calculations for individual groups of patients treated in facilities of the treatment-and-prevention system.

In the overwhelming majority of stomach cancer patients (93.1%), surgical intervention has been the only treatment method. Of a total of 1,285 stomach cancer patients chosen for study, 753 underwent surgery. The observed five-year survival rate of patients who received only surgical treatment for localized disease (stages I and II) and diffuse disease (stage III) was, for men, 66.7% and 16.1%, respectively, at the SRI Oncology; 50.8% and 20% at the Leningrad City Oncology Clinic; and 58.3% and 33.3% at the other facilities. For women, those figures were 56.2% and 17.3%, 57.1% and 13.2%, and 33.3% and 20%.

The observed five-year survival rate associated with the so-called radical treatment**** of rectal cancer in men was, for localized disease and diffuse disease, 45.4% and 44.3%, respectively, at the SRI Oncology; 25.0% and 22.7% at the Leningrad City Oncology Clinic; and 29.4% and 29.4% at the other facilities. For women, those figures are substantially higher: 62.5% and 42.2% at the SRI Oncology; 70.0% and 34.8% at the Leningrad City Oncology Clinic; and 54.2% and 18.2% at the other facilities. Interestingly, the outcomes associated with the five-year survival rate following radical treatment of rectal cancer at the Leningrad City Oncology Clinic coincided completely with those published by the National Cancer Institute in the United States—69% and 36%.⁸

The figures for the five-year survival rate associated with the radical treatment of lung cancer in men at permanent oncology facilities are similar: 37.8% for localized forms and 25.3% for diffuse disease at the SRI Oncology, and 43.3% and 30.8% at the Leningrad City Oncology Clinic. These figures are not calculated at other facilities or for women, because of the small numbers of individuals observed.

In a study of the outcomes of the medical care given to breast cancer patients in various types of permanent facilities, 1,388 patients were tracked, 97.7 of whom received special treatment. A total of 40.2% underwent surgery; 33.4% underwent combined treatment; 20.5% underwent complex treatment. The five-year survival rate observed with the combined method of treatment for localized forms of the disease was 82.3% at the SRI Oncology, 64.9% at the Leningrad City Oncology Clinic, and 52.6% at the other facilities.

Those who underwent radical treatment for breast cancer at the SRI Oncology had a five-year survival rate of 73.3% for localized forms and 51.1% for diffuse forms; the figures at the Leningrad City Oncology Clinic were

65.9% and 41.9%. Comparison with the outcomes in the general treatment-and-prevention system among the group of patients with diffuse forms of the disease is erratic, because categorization among most of the patients does not meet today's requirements. According to the data of D. P. Berezkin and colleagues,² the figure for the survival rate observed among breast cancer patients treated at 26 oncology facilities in the USSR (1974-1980) is 55%.

Cervical cancer is traditionally treated in specialized oncology facilities. Of 609 patients in the study, only 44 were treated outside the specialized system. The small number of observations did not make it possible to include this group in the comparative analysis of treatment effectiveness. At the SRI Oncology, the figure for the survival rate observed with this oncological form was 66.1%; at the Leningrad City Oncology Clinic, it was 52.6%. According to the data of the U.S. National Cancer Institute,³ the relative five-year survival rate of cervical cancer patients is 59%. The outcomes associated with the five-year survival rate among cervical cancer patients who undergo radical treatment at the SRI Oncology are 74.8% and 38.5% for localized disease and diffuse disease; at the Leningrad City Oncology Clinic, they are 69.4% and 25.0%.

Cancer of the corpus uteri is also treated primarily in specialized oncology facilities. Radical treatment of this form of cancer produces five-year survival rates of 75.7% and 40.0% for localized and diffuse forms at the SRI Oncology; the figures are 77.5% and 46.7% at the Leningrad City Oncology Clinic. It can be said that the figures are rather high.

The leading form of treatment for ovarian cancer (among 457 observations) is combined treatment (51.1%), second place belongs to the chemohormonal method (18.5%), and third belongs to surgery (14.0%). The survival rate associated with localized forms of ovarian tumors is growing appreciably. At the SRI Oncology, for example, it is 82.4%; at the Leningrad City Oncology Clinic, 92.9%; and at the other facilities, 57.2%. For diffuse disease, the figures are 71.4%, 46.7%, and 25.0%.

Conclusion. The analysis we conducted touched on only some of the outcomes of treatment rendered to oncology patients in permanent facilities in a large city. The indices and structure of morbidity among the population has an undisputed effect on the nature of oncology care in a large city. The morbidity figures for Leningrad residents between 1970 and 1986, for example, are consistently higher than for the USSR as a whole, the RSFSR, and Moscow.

The organization of oncology care in large cities has its own features, which often do not fit into the customary scheme of things. In Leningrad, a great many of those with a first-time diagnosis are hospitalized immediately in the facilities of the general treatment-and-prevention

system. An analysis of the distribution of patients hospitalized in oncology facilities and facilities of the general treatment-and-prevention system indicates convincingly that the more seriously ill oncology patients (with stage IV forms) are hospitalized in general treatment beds (stomach cancer, 51.9%; lung cancer, 42.6%; cervical cancer, 34.9%; and ovarian tumors, 40.9%).

Thus, every second or third patient (depending on the tumor site) is admitted in permanent hospital facilities of the general treatment-and-prevention system in stage IV of the disease.

Undisputed results have been produced by the multiyear organizational work directed at getting patients who need combined or complex therapy sent to specialized facilities. One basic issue involves the criteria that characterize malignant neoplasms. This pertains to morphological verification of the disease process and determination of degree of its diffusion (the disease stage). In treatment-and-prevention facilities (regardless of the site of the disease process), those indices can not be judged satisfactory. In stomach cancer patients treated in facilities of the treatment-and-prevention system, for example, the diagnosis is verified morphologically in only 39.7%, whereas this figure is substantially higher in specialized facilities (82.2% for the SRI Oncology and 63.8% for the Leningrad City Oncology Clinic).

The analysis conducted showed that in facilities of the general treatment-and-prevention system, the stage of the disease process is not established in 20-30% of the cases; for some sites (cancer of the corpus uteri, lung cancer, and cervical cancer), those figures are considerably higher, at 51.3%, 29.0%, and 25.6%. The explanation for this should probably be sought in the fact that a rather large percentage of patients (12.5% for stomach cancer) present with emergency indications; moreover, as was noted, it is in the facilities of the general treatment-and-prevention system that the principal contingent of patients in stage IV of the disease process are concentrated. In addition, in a great many cases, there is some doubt about the correctness of the determination of stage, since, judging from patient history data, some of the stage IV patients undergo so-called radical treatment.

The issue of morphological verification of diagnosis in various kinds of treatment facilities merits special attention and study. In correctly noting that morphological verification of diagnosis in facilities of the general treatment-and-prevention system cannot be judged satisfactory, we can't help but say that that the level of verification in specialized facilities does not meet today's requirements.

The outcomes associated with observed survival rate indicate that surgical treatment performed in certain facilities does meet today's requirements. This is true, primarily, for the highly advanced clinics of the medical and scientific research institutes, the concentration of which is especially great in the large city.

Additional detailing of the information received and in-depth expert analysis are needed to develop a complex program for improving the oncology care rendered to the residents of a large city.

This first experience in studying the observed survival rate of oncology patients treated in the various kinds of facilities in a large city makes it possible to conclude that there is a need for this kind of work on a systematic, daily basis. For that purpose, an effective, high-capacity organizational and information center is needed for collecting, assembling, storing, and promptly analyzing the situation with regard to identification, treatment, and clinical observation of patients with malignant neoplasms.

Footnotes

*In all, in 1982, in Leningrad there were 14,337 first-time diagnosis patients, 1,226 of whom refused treatment; oncology patients accounted for 31.2% in the selected study.

**A great deal of help in preparing these materials was given by staff members of the city oncology clinic, rayon oncologists, physicians from rayon oncology departments, and workers at the medical archives of the treatment-and-prevention facilities, at the documentation division of the central address bureau, and at the rayon departments of the civil registrar's office.

***The research effort included information pertaining only to patients in whom there was morphological verification of diagnosis and determination of stage of disease process.

****Because analysis of the data was done on retrospective material in this work, the assessment of the degree of radicalness of the treatment was rather problematic. This circumstance was further aggravated by the large number of clinics and the differing approaches in them to assessing the radicalness of treatment.

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Concern Over Chernovtsy Thallium Poisoning
18400434 Moscow SOTSIALISTICHESKAYA
INDUSTRIYA in Russian 23 May 89 p 3

[Article by V. Popkov: "A City Without Children's Laughter"]

[Text] "This is already the eighth month that children are ill for some unknown reason in the city of Chernovtsy and the towns surrounding it. They are suffering from disorders of the nervous system, disrupted functions of the internal organs; some are losing their hair partially or completely... According to the data of the oblast epidemiology and public health service, in February, 1989, there were 96 such cases, and over 20 days in March, already 66..."

These are lines from a letter sent 21 March to the Presidium of the USSR Supreme Soviet, the World Health Organization, the Executive Committee of the Union of Societies of the Red Cross and Red Crescent. Nine thousand residents of Chernovtsy and the oblast have placed their signatures under it.

Much was written about the tragedy in Chernovtsy in the fall of last year. Then, other events got rolling. And the remote western Ukrainian city receded to the background. It could have seemed that the misfortune had passed. And a reprise of the mysterious illness, judging by the information in the central press, was "highly improbable, as a result of the wide-scale work in sanitary purification...ecological conditions in the city have returned to normal."

No, however, they have not returned to normal. And they could not return to normal. After all, nothing was done to remove the real reason for the illnesses.

Yes, the city was actually washed, and cleaned; all the grass was dug up just in case. Control of the wastes of industrial enterprises was tightened; several were even closed down. The issue of providing Chernovtsy with unleaded gas was resolved expediently. Measures such as these could restore health to the ecological condition of any populated area. And they yielded a definite positive effect in Chernovtsy. But all this is strongly reminiscent of washing the floor in the patient's room: it is useful, but it has nothing to do with the cure.

Unfortunately, the source to the misfortunes has not yet been found or identified.

"How can that be?" ask those who remember the events of November of last year. "But what of the thallium that there was so much talk about?"

But the thing is that there was far more talk about thallium, it seems, than there actually was thallium detected.

Judging by appearances, one of the first to utter the name of this fairly exotic metal in late October was Professor V. Tatochenko of the Moscow NII [Scientific Research Institute] of Pediatrics and Pediatric Surgery, who investigated the children evacuated from Chernovtsy. Essentially, he uttered it on the basis of the picture of baldness classic for thallium. The professor's position is understandable: in order to begin treatment, he had to proceed from some sort of plausible version. Since he was only a pediatrician, and not a toxicologist or chemist, of course he did not claim to have established a final diagnosis. However, the prompting of the Moscow professor proved to be extremely opportune.

Judging by appearances, back in the beginning of November, the commission from the USSR Ministry of Health working in Chernovtsy did not have a clear opinion. Thus, in the oblast newspaper, RADYANSKA BUKOVINA of 5 November, the Deputy Director of the USSR Ministry of Health confirmed that "We are inclined toward a fungous version... Two thousand dogs were caught; among them we found one bald one... We are waiting for news from Moscow, where the samples were sent..."

And by 9 November, at a press conference, Minister Ye. Chazov expressed his opinion of the possible participation of acid rains. True, they spoke of them only as a means for delivering ...thallium. And all effort was put into the development of the "thallium version."

Interesting information can be derived from the log of telephone conversations at the USSR Ministry of Health. These were holidays, but the people were not up to revelry. Scientists from the USSR Academy of Sciences Institute of Organic Chemistry in Kiev were the first to register elevated thallium content in the samples, on 8 November, at 11:40. A. Baranov called from Chernovtsy at 13:40 to report of the detection of thallium by Kiev State University and the Uzbek SSR [Soviet Socialist Republic] Academy of Sciences Institute of Nuclear Physics in Tashkent. Then, at 15:15, the Moscow VNII [All-Union Scientific Research Institute] of Applied Molecular Biology and Genetics telephones that "the research results indicate thallium." Finally, on 9 November at 14:00, a call from Kiev, from A. Pavlov, director of the VNII of Hygiene and Toxicology of Pesticides, Polymer and Plastics of the USSR Ministry of Health: It is thallium!

For the sake of objectivity, it should be said that the research conducted led in different directions. According to the members of the commission, however, the viral, radiation, alimentary and, medicinal versions crumbled one after the other. They held onto the chemical version somewhat longer. But even this was overturned due to a lack of evidence.

True, other voices mixed in with the general "thallium chorus." On that same eventful day of 8 November, specialists from the Institute of Experimental Meteorology in Obninsk—the leading scientific center of the State Committee for Hydrometeorology—inform the Ministry of Health that they had not managed to find any signs of anomalous thallium content in the water and soil samples received from Chernovtsy. And researchers from the Institute of Atomic Energy imeni I.V. Kurchatov [IAE] did not detect thallium in the biological samples. One day earlier, on 7 November, at 8:25, a call came through to the duty phone at the USSR Ministry of Health with news from the Ministry of Internal Affairs [MID] VNII that should have at least put people on guard: a manifold elevation of boron concentration had been detected! These conclusions were later confirmed by IAE as well. But the commission members did not perk up their ears...

Why not? At that moment, by degree of probability and by the authority of the scientific institutions promoting both, the thallium and the boron versions appeared to be equally valid. Nevertheless, preference was given to only one.

I understand that it was necessary to somehow calm down the terror which plagued people. I am prepared to believe that there was no time for the development of

two alternative versions—all eyes were turned upon the Ministry of Health. Just let even the thallium version, as it happened, become the official one, and it entered the act of the government commission. But the commission members, "for themselves," were required to continue to have doubts. All the more so because they were extremely well-founded.

The commission's act itself indicated the possible source for the thallium's ingress into the environment: home-made anti-knock gasoline additives. A. Baranov, in his televised speech at the end of November, spoke of this in particular: "...It is the opinion of our commission that this is nevertheless gasoline." But the specialists on automotive fuels with whom I spoke would only shrug. "I have never heard of using thallium in that capacity," said with surprise V. Yemelyanov, manager of the gasoline technology laboratory of the VNII for Oil Processing. "I have never come across an idea like that even on the purely patent level."

Isn't this why the act taken in November is somewhat blurred? In it I read, "The probability of toxic influence of a low dose of thallium against a background of certain ecological violations can be admitted." And a number of questions immediately arise. What "low doses" (?) are they talking about? What are "certain violations"? And what has thallium got to do with it when it is acknowledged on the same page of the act that the Chernovtsy disease "does not fall into the pattern of acute or chronic thallium poisoning in doses exceeding allowable limits, as described in the literature"?

In spite of this, the Ministry of Health grabbed for the thallium version like a life preserver. And it stands by this version to this day, as they say, to the death. But children remain ill in Chernovtsy. And the adults have become more embittered, seeing that in general, they have been left one on one with misfortune.

You will agree: it would be much more honest and humane not to instill people with groundless hopes for a quick correction of matters, but to explain all the complexity of the search for the real reasons for the misfortune, to call upon the Chernovtians as allies. For most responsible workers, a burdensome inconvenience was held in this seemingly most logical step; it obliged them to act and make serious decisions. Strength and resources would be required in order to expand the search for this sinister reagent, in the full sense of the word and across the entire front, including the search for boron as well. The entire population would somehow have to be made safe. And at the very least, the children would be evacuated.

Complicated, expensive? Yes. And there is the danger that your steps will be considered excessively zealous. Wouldn't it be simpler not to take them? That sort of position only threatens to exacerbate the misfortune.

The evacuation, let us say, began without any orders. The price of tickets privately available to nearby Lvov jumped more than five-fold, and reached R50. But nevertheless, according to the data of RABOCHAYA GAZETA, by 19 November, of the city's 15,000 preschool children, 559 remained; and of the 33,000 schoolchildren, 5,000 remained.

The spontaneous export of children began at the end of October, when the newspaper reported on the strange epidemic of unclear origin. But the city authorities did not even attempt to channel the evacuation, to direct the children to one place. Only the railroad workers' trade union did this in an organized manner. And at that time, neither the mycological nor the infectious versions had been completely discarded. It is terrible to even think about the misfortune the children from Chernovtsy could spread through the entire country if this turned out to be an infectious disease.

This graphic example bears witness to how clumsy we are in the event of disaster. In order to calm people, we create commissions with splendid "government" titles, and we draw into them major leaders and specialists. But specialists in their own fields of constant work. I fear that many of them have a poor idea of how to act in critical situations, what measures to take, whom not to admit and where not to admit them, whom to help first. We survived some stage of helplessness in Chernobyl, and the necessary system was established in Armenia far from quickly.

Ecological catastrophes are no less horrible. And in today's world, most likely, they will be repeated fairly often. It seems that in the struggle against their consequences, a well-equipped and trained emergency service is needed, composed of the most disparate specialists. Even up to military specialists capable of maintaining order, and bringing in troops having access to defense secrets. This service cannot belong to any department or express its interests. It must answer only to the government.

The USSR Ministry of Health held a series of conferences on Chernovtsy in March. In April, after many months of agreement, two experts from the World Health Organization visited the city. But they could not say anything definite either, as they have relied upon the information given to them by the Ministry of Health. The experts left perplexed. And a strange and terrible indifference reigned over the city's situation once again, although this serious ailment continues its pernicious harvest. But the dissatisfaction of the city's residents has reached a critical point. They feel completely helpless. It is impossible to reach the truth, impossible to extend a certificate of medical leave, impossible to get a new one. But this is not the only thing. A city without children, a city without children's laughter—what could be more unnatural?

Soviet Pharmaceutical Industry: Present State and Future Prospects

18400447 Moscow *ADVANCES OF SCIENCE AND TECHNOLOGY* in English No 3, 30 Jan 89 pp 1-5

[Interview by APN correspondent with Valery Bykov, Minister of the USSR Medical and Microbiological Industry]

[Text] An additional 5.6 billion roubles is to be allocated from the budget in the next three years for the development of the Soviet health services under a new state program. Part of this sum will be used for the rapid development of the drugs industry.

Valery Bykov, Minister of the Medical and Microbiological Industry of the USSR, talks to an APN correspondent about the problems and prospects of the industry.

Question: About 3,000 drugs are entered in the USSR State Pharmacopoeia. To what extent is your ministry, set up in 1985, satisfying the population's demand for these medicines?

Answer: Ninety-seven per cent of the medical preparations in the country today are manufactured by our ministry. Of the 3,000 mentioned, we fully satisfy the demand for 1,300, and by 90 per cent for 800 others. Two hundred preparations are made in amounts that meet just only 70 per cent of the requirements, and in a number of drugs we are badly down. This applies first to psychotropic preparations and medicines to treat cardiovascular diseases. Some of these preparations are imported, with purchases done in CMEA (Council for Mutual Economic Assistance) countries under long-term agreements on production specialization. This makes up more than 90 per cent of all our imported medicines and costs about a billion transferable roubles annually /the transferable rouble is a money unit adopted for dealings between CMEA member-countries/. A number of drugs are bought in Yugoslavia, Finland, India and some other countries. This year's imports of some drugs, above all cardiological ones, have grown considerably. Purchases of cordarone from Yugoslavia have increased by almost 150 per cent compared with the past. Much more corinfar is being bought in the GDR, and with additional deliveries of this drug, now labelled as cordafen, from Poland demand for this effective preparation will be met in full. In addition to long-effect nitroglycerin, some new medicines are being purchased from Poland - mitte and forte sustonit.

Demand for them is satisfied in full. A new form of buying is being tried out. In Yugoslavia, for example, we purchase granulated semifinished products to manufacture the necessary medicines in the Soviet Union.

Question: The USSR Council of Ministers in a decree obliged you to fully meet demand for basic drugs by 1993. Is that feasible? And to what extent will the attainment of this objective rely on the country's own production potential?

Answer: Honestly, we have a lot of problems. Our machine-building industry is lagging behind and we have to produce some of the drug-making equipment at our own enterprises. We also need packing and ampoule filling lines. Even so I do hope that we shall cope with the task. And primarily by developing the Soviet pharmaceutical industry.

This is evident from the rates of growth of our output, which in the current five-year period reached more than 8 per cent.

Question: The drug industry in some advanced countries is the second most profitable branch, after arms production. What about you, what is your budget?

Answer: In this country the pharmaceutical industry is not a line of business. We cannot allow high prices prevent drugs from reaching some of the population. Take, for example, validol or nitroglycerin, the most widely used preparations against heart diseases. One package of these drugs costs 8 and 13 kopecks, respectively. But their manufacture is much more expensive. In the same way, some 400 more preparations incur a loss. We finance their manufacture with profits from other drugs. Our industry has the minimum turnover tax to make production profitable. And we are already raising the question of putting our industry on a self-paying basis. We have three sources of financing: first, state centralized investments; second, the funds of enterprises; and third, part of the profits made by the industry. It is with this money that we are building new plants and modernizing old ones.

Question: What is the procedure in the Soviet Union for getting permission for the manufacture and use of a new drug?

Answer: This is the business of the Pharmacological Committee of the USSR Health Ministry - an expert organization that examines before clinical use new preparations proposed by scientific organizations or individual authors. The Committee has on its staff leading toxicologists and scientists from the Institute of Pharmacology and from the Research Institute of Technology and Safety of Medical Preparations. They study the side effects of medicines. The obligatory investigation of each medicine includes the study of its influence on the immune system, its mutagenic properties, its ability to cause an allergy, its effect on the development of a fetus, and lastly, its long-term effects on the development of the body itself. The Committee receives some 200 to 240 Soviet drugs and between 240 and 360 foreign ones annually. The first screening leaves only one-third to be

clinically tested, while the others, if these are Soviet-made preparations, are sent back for updating. It is only four to five medicines that are approved for use following these comprehensive tests.

Under a new procedure, the testing of a drug must consist of three stages. The first, or pilot scale, stage involves the administration of the preparation to 10 or 20 patients to see how well it is tolerated and its likely side effects. At the second stage, the medicine is investigated at two to three clinics on 30 to 50 cases. The final stage includes its use in 6 to 10 clinics on 100 to 150 patients. Following thorough studies, its final destiny is decided. And even after the drug is put into regular production, the Committee keeps an eye on it, in the event of a possible side effect that may display itself after a long while.

Question: What proportion of Soviet medicine is made from vegetable sources?

Answer: Almost 40 per cent. We have a special association for vegetable raw materials - the Soyuzlekrasprom agroindustrial organization. Since the demand for medicinal raw materials is growing all the time, the organization is expanding too: over the last two years we set up seven new state farms to raise medicinal plants. All in all, there are 36 of them in the country. They cultivate over 100 plants.

In addition, expeditions of the All-Union Institute of Pharmacological Plants go to most remote parts of the country in search of wild-growing medicinal herbs. The plants found are analyzed for bioactive substances and, if the analysis is positive, methods are developed to cultivate these plants on industrial plantations in definite climatic zones.

I wish to note that most of cardiological medicines today are of vegetable origin. In spite of advances in fine organic chemistry, there still are no substitutes. Besides, unexplored wild-growing plants have a very high potential. Recently, one plant - white-mouthed aconite - was found to contain some cardiac glucosides possessing a high antiarrhythmic action. As a result, the Tashkent Institute of the Chemistry of Plant Substances has developed a technology for obtaining two quite new preparations - allapenin and alsumin. These have undergone clinical tests and have been recommended for extensive medical uses.

Question: What preparations of world standards are about to be launched by the Soviet pharmaceutical industry?

Answer: I would like to single out the group of thymidines obtained from the milt of sea fishes by the research and production organization Biotechnology under Doctor of Biology Anatoly Stepanov. These compounds serve as a raw material for the production of

azidothymidine used to enhance human immunity especially in AIDS cases. The preparation, after successful tests in the Soviet Union, is being handed over to Finland, while we are arranging with American scientists to test more active compounds from the thymidine group and to jointly develop industrial-scale technologies for their manufacture.

Genetically engineered insulin is being put into regular production. This work is shared on a competitive basis by some sectoral research institutions, the USSR Academy of Sciences and the All-Union Research Institute of Antibiotics. This preparation will be of the time-release sort. Combined with polymer film, it will be evenly absorbed through the skin in carefully time-determined doses. This will dispense with the need to administer insulin by injection.

Incidentally, polymer films - a new medicinal form - will be used widely with other preparations. Imagine a sticky platelet attached to a heart wall in patients suffering from stenocardia.

Industry is already producing yet another cardiological preparation developed by Soviet scientists - trinitrolong. It is enough for this small film to be placed under the tongue for the medicine to enter the body regularly in the course of several hours.

Among other preparations is violosen (with antiallergic action), furosemid, a potent diuretic, and prazolin, a drug blocking adrenoreceptors.

In the group of promising drugs we find the preparation called mildronat, which was developed at the Institute of Organic Synthesis of the Latvian Academy of Sciences. It is an analog of alanine, an essential amino acid that regulates biochemical processes, increases activity of enzyme systems and metabolic processes. At first mildronat was proposed as an anti-ischemic medicine, to treat congestion in hypertension, as an anti-ulcer preparation, a drug in the combined treatment of diabetes, and as an anti-viral drug. Its clinical tests were successful. Mildronat also increases the vigour of the body, improves memory, develops speech habits, and is effective in treating impotence.

The joint development of the antiarrhythmic preparation bonekor by Soviet and East German pharmacists was successful, too. The drug formula was developed by Soviet scientists, while the output of necessary substances was organized by German colleagues. The clinical examination of the medicine was conducted simultaneously in two countries. Bonekor, as distinct from previous drugs, has no side effects. Patents for it have already been taken out in some countries. The American firm Ely Lilly has concluded a contract and will take delivery of this preparation.

The tranquilizer sermion is being prepared for production in the USSR jointly with the French firm Rhone-Poulenc, while with the Swiss Sandoz, the drug to be made is parlodelum, a preparation stimulating lactation in nursing mothers and improving metabolism.

Question: What other foreign pharmaceutical firms have equally active relations with you?

Answer: The most fruitful contacts have been with the Swiss firm Hoffmann-La Roche. Since the new year we have set up a joint venture with it to produce diagnostic sets for enzyme immunoassays. At present we have a critical need for them.

Another joint venture is going to be initiated with the American firm Upjohn. The aim is to make psychotropic drugs.

Fruitful cooperation is also developing with such firms as Fresenius from West Germany, Solco from Switzerland, and some others.

Question: What are the prospects for joint ventures in the next five-year period?

Answer: I believe their number will increase by at least ten by 1993. In conclusion, I would like to stress that we ourselves will be establishing more than a hundred new processes at forty factories to meet in full public demand for medicines in both range and amount.

UDC 615.849.1/.2.015.25(035) (049.32)

**G. A. Zedgenidze Reviews Book on
Radioprotectors**
*18610297 Moscow MEDITSINSKAYA RADIOLOGIYA
in Russian Vol 33 No 11, Nov 88 pp 77-78*

[Review by Academician G. A. Zedgenidze, USSR Academy of Medical Sciences, of "Radioprotektory (spravochnik)" [Radioprotectors (A Reference Book)], by V. S. Gugushvili, I. M. Dzhandzhgava, Z. D. Kakhiani, K. Sh. Nadareyshvili, O. N. Saneblidze, and M. N. Khurtsiya, Tbilisi: Metsniyereba, 1987, 472 pages]

[Text] This 472-page reference book is devoted to a very important problem—protecting living organisms against radiation. The book contains materials published in the USSR and abroad between 1965 and 1985 that deal with the study of pharmacochemical agents increasing the organism's radiation resistance. As the authors rightly stress in their foreword, similar domestic and foreign publications were published during the sixties, and the data presented in the book being reviewed here are thus distinguished by their innovation, reflecting the current status of the problem. That is true especially since it includes information dealing with the mechanism of action of the most-studied drugs and chemical compounds. It can therefore be boldly stated that this edition of the book being reviewed is unique.

Besides a foreword, the reference book contains three independent sections, a bibliography, a list of abbreviations, and a subject index. The independent sections deal with the following: medications to prevent radiation injuries (276 pages), the combined use of agents for preventing radiation injuries (71 pages), and the clinical use of certain antiradiation protective agents (8 pages).

All of the sections are laid out in the same manner. The text is presented in two columns. The left-hand column contains the drug or chemical name, dose, time and method of administration, and type and dose of radiation. The right-hand column contains the object under investigation, the characteristics of the effectiveness of radiation protection, and a bibliographic source citation.

This method of presenting the material is very convenient for a reader who is searching for needed sources within an extensive amount of information about radioprotectors. As the authors note, the reference book does not contain any information about research on physical means and methods of protecting against radiation (aeroionization, electromagnetic fields with different frequency ranges, etc.). The mechanisms of their effect are unclear, and their results are debatable.

The bibliography and, consequently, all the published works amount to almost 1,500 sources, which in and of itself confirms the abundance of information and the difficulties in getting oriented in it without an appropriate reference book. The well compiled subject index, which is 15 pages long, provides the necessary help in finding needed information.

The authors have thus collected and systematized the enormous amount of material on pharmacochemical radioprotectors that has been published both in our country and abroad, which undoubtedly required a great deal of effort, painstaking labor, and skill. The book is a valuable reference aid for radiobiologists and radiologists, hygienists and radiation therapists, a wide range of physicians, and research associates interested in matters related to radiation protection.

The materials presented in this reference book will make it possible to avoid superfluous searches and to efficiently plan scientific research work in this area of practical import.

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UDC 616.988.25+547.963.3

Oligonucleotide Derivatives Complementary to Viral RNA Inhibit Reproduction of Tick-Borne Encephalitis Virus In Cell Culture

18400053c Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 301 No 5, Aug 88 (manuscript received 1 Mar 88) pp 1257-1260

[Article by V. V. Pogodina, T. V. Frolova, T. V. Abramova, V. V. Vlasov, Ye. M. Ivanova, I. V. Kutyavin, A. G. Pletnev and L. A. Yakubov, Institute of Poliomyelitis and Viral Encephalitis, USSR Academy of Medical Sciences, Moscow oblast; Novosibirsk Institute of Bioorganic Chemistry, Siberian Division, USSR Academy of Sciences]

[Abstract] The problem of producing effective antiviral preparations remains the most pressing in viral infection therapy. One new approach in this direction is based on selective damage to or blocking of the functioning of the viral genome using oligonucleotide derivatives complementary to sequences of viral nucleic acid. There is particular interest in the use of alkylating oligonucleotide derivatives to chemically modify target nucleic acids that not only have an inhibiting effect on viral reproduction or a modulating effect on mRNA cell activity, but also create conditions for detailed study of intracellular interactions of nucleic acids. In order to clarify the feasibility of using a reactive oligonucleotide derivative of a given sequence to suppress reproduction of tick-borne encephalitis virus in a cell culture, the researchers examined the effects of oligonucleotides pT (CT)₆, complementary to a viral RNA polymerase gene sector, and pT₁₆, complementary to a viral RNA poly-A sequence, on a high virulent strain of the virus. The oligonucleotide derivative CIRpT (CT)₆ and its unreactive analogue (OH) RpT (CT)₆ were found to have a clear inhibiting effect on viral reproduction. The inhibiting effect decreased by less than one order of magnitude with a decrease in reagent concentration from 100 to 1 μ M. It is thus demonstrated for the first time that oligonucleotide derivatives complementary to a functionally important viral RNA sector have a detectable inhibiting effect on reproduction of the virus in cell culture. The effect is dose-dependent and highly specific. References 14: 8 Russian, 6 Western.

UDC 578.842

Reproduction of Blue and Orange Iridoviruses of Aedes Aspius Caspius In Bombyx Mori Larvae

18400057a Kiev MIKROBIOLOGICHESKIY ZHURNAL in Russian Vol 50 No 3 May-Jun 88 (manuscript received 16 Feb 87) pp 89-92

[Article by Kh. K. Torybayev, Institute of Microbiology and Virology, Kazakh Academy of Sciences, Alma Ata]

[Abstract] Entomopathogenic viruses must be accumulated for study. One convenient method of accumulating large quantities of viruses is their reproduction in laboratory cultures of susceptible insects. This article studies

the possibility of reproduction of *Aedes aspius caspius* iridoviruses in the larvae of *Bombyx mori*. The results of the experiment showed that infection of the larvae caused them to lag in growth rate, taking on an irregular bluish violet spotty color before dying. A few managed to produce a thin, irregular cocoon, but most died before reaching that stage. A total of 77 percent of the larvae inoculated with the blue iridovirus died, as did 92 percent of the larvae infected with the orange virus. Most of the deaths came between 9-22 days after infection. The results indicate that the iridoviruses of *Aedes aspius caspius* can easily accumulate in the body of *B. mori* when they are infected by injection in the hemocele, with reproduction of the viruses observed in the cytoplasm of the cells in a number of structures in the larvae. Figures 5, references 5: Russian.

New Stage In AIDS Study

18400057b Moscow PRIRODA in Russian No 5, May 88 pp 60-63

[Article by A. Ya. Kulberg, doctor of medical sciences, Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow]

[Abstract] The key to the pathogenic effect of the AIDS virus may lie in the biochemical properties of the proteins of the virus embedded in its wall. Any virus causing AIDS has the unique protein gp160 in its wall. The most important function of this protein, present in many thousands of copies on the surface of the virus, is to attach the virus to cells sensitive to the protein, after which the virus penetrates the cells. This viral protein is similar to human cell wall proteins. The researcher compares protein gp160 with one of the most important human cell wall proteins, the growth hormone receptor. One portion of the protein, referred to as gp120, has two bean-shaped compact structures that are similar in size; the domains that form gp120 are quite similar to the domains of the growth hormone and insulin receptors located in their "recognition" sectors. In the laboratory, the researcher had previously shown that a wide variety of receptor proteins embedded in human and animal cell walls have structural elements that are similar to those of gp120. Such cells are constantly discarding portions of receptors that are attached to their outer surface—receptor molecule fragments that the researcher calls R-proteins. The gp120 sector is also spontaneously cast from the surface of the viruses that cause AIDS, leaving a "bald spot" on the surface. A clear similarity was found between the viral protein and other receptors as well as serum immunoglobulin in terms of the structure of the gp120 domains and those of the highly conservative, extracellular amino acid sequence sectors of a number of human protein receptors. Such sectors are antigen determinants, to which antibodies can be produced. These antibodies, which are called "antivariotypical antibodies," interact with the cell receptors and block their active centers. The highly conservative sectors the researcher discovered in the structure of gp120 are

similar to those of the cell receptors and immunoglobulin, not only in their chemical structure, but also in their antigen structures. Which means that the antigen determinants of the AIDS virus proteins are similar to the receptor protein determinants. In persons infected with the virus, antibodies appear that interact with gp120. One peculiarity of the immune system, however, is that it can become confused and turn against its own cells and tissues. That is what happens with the protein sector gp120, since it is both similar to the receptor cell proteins of the infected individual and yet foreign. Antibodies are generated against both the patient's own proteins and the foreign proteins. These antibodies begin to block various receptors, including the T-helper receptors, thereby suppressing the immune response. The receptors of other cells that "recognize" hormones and tissue growth regulators, for example, are also blocked. Recent monkey experiments in the United States showed the damaging effect of the virus to be greater, for this reason, in animals vaccinated against AIDS than in nonvaccinated animals. The Laboratory of Immunochemistry of the Institute of Epidemiology and Microbiology imeni N. F. Gamaleya determined that the R-proteins play a key role in regulating biological equilibrium, the disruption of which is the main disease factor. Essentially, R-proteins are internal toxins that "capture" hormones and various nutrient substances needed by cells and catalyze peroxide oxidation. HIV proteins are biochemically similar to R-proteins, meaning that gp120 can apparently suppress immunity and weaken the biosynthesis of a wide variety of substances, completely exhausting the patient's body. Antibodies against the virus merely accelerate the breakdown of gp160 to gp120 and fragments similar to R-proteins. They react with the patient's cell receptors to accelerate the discarding of all the new R-proteins from the cell surface, which in turn has a toxic effect on the body and suppresses immunity. New data from the institute indicate that the activity of R-proteins in AIDS patients is 50-100 times greater than in the serum of healthy individuals. The process occurs as follows: the virus enters the body; it multiplies in sensitive cells; it exits the cells, at which point gp120 is discarded from its surface; the immune response occurs; antibodies appear, reacting both with gp120 and various cell receptors of the individual; these antibodies block the receptors of T-helpers and other cells.

UDC 615.33:578.245.2:[615.451.234:547.953

Antiviral Activity of Amyxin Incorporated Into Liposomes

18400058b *VOPROSY VIRUSOLOGII* in Russian
Vol 33 No 3, May-Jun 88 (manuscript received
8 Jul 87) pp 302-305

[Article by S. S. Grigoryan, A. N. Simonov, A. M. Ivanova and F. I. Yershov, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

[Abstract] Amyxin is a Soviet analog of tilorone, a highly active interferon inducer with a broad spectrum of antiviral action. In a search for the best means of clinical use of amyxin, researchers compared the effectiveness of its use (both free and incorporated into liposomes) in experimentally induced enteral and parenteral hepatitis in 16-18 g male mongrel mice weighing 16-18 g. The

amyxin—2,7-bis-(2-dimethylamino)-ethoxyfluorenone-9 dichlorohydrate—was synthesized at the Physico-chemical Institute of the UkrSSR Academy of Sciences. Test viruses included the Indiana strain of vesicular stomatitis virus and the Meshcherin strain of mouse hepatitis virus. A single injection of amyxin without liposomes did not produce antiviral resistance when the mouse hepatitis virus was administered intraperitoneally. Amyxin incorporated into liposomes afforded only negligible protection. The antiviral action was markedly higher in the enteral hepatitis, especially with amyxin in liposomes. The research findings point the pronounced antiviral action of prophylactic peroral use (24 hours before infection) of amyxin incorporated into liposomes, with the use of the newly developed model of experimental enteral mouse hepatitis. The procedure produced a 60 percent survival rate and a 2.6-fold increase of life-span of the mice. The beneficial effect was attributed to both the method of administration of the inducer and its incorporation into liposomes. It was assumed that amyxin and then the virus follow a similar pathway in the body, and the amyxin induces interferon production in the liver and spleen and prevents virus reproduction. The results show promise for the use of amyxin incorporated into liposomes in clinical tests on humans to prevent hepatitis A. References 14: 4 Russian, 10 Western.

UDC 615.373:578.833.26].03:616-078.73

Production and Properties of Monoclonal Antibodies to Pichinde Arenavirus

18400058c *VOPROSY VIRUSOLOGII* in Russian
Vol 33 No 3, May-Jun 88 (manuscript received
28 Nov 86) pp 365-369

[Article by L. Ya. Kunitskaya, I. V. Malakhova, S. I. Bystrova, N. N. Lemeshko, A. S. Vladko and A. S. Novokhatkiy, Belorussian Scientific Research Institute of Epidemiology and Microbiology, BSSR Ministry of Health, Minsk]

[Abstract] Development of optimal conditions of producing monoclonal antibodies to Pichinde virus was described and discussed. Indirect immunofluorometry (IIF) was used to make a preliminary analysis of the specificity of the antibodies for protein viruses. Titration of the Pichinde virus antigen was performed with solid-phase enzyme immunoassay (SEIA), and a more detailed analysis of the antibody specificity for the structural proteins of the virus was done with immunoprecipitation. All monoclonal antibodies appeared to be specific for surface glycoproteins of Pichinde virus. IIF showed the titers of the monoclonal antibodies to vary from 1:256 to 1:1024, and SEIA showed them to vary from 1:64,000 to 1:10,000,000. Their avidity was A-2 is less than A-3 and greater than A-1. It was found that when monoclonal antibodies are included in diagnostic test systems at the "second antibodies" stage of indirect EIA, it is advisable to use monoclonal antibodies A-3. Figure 1; references 16 (Western).

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